Technical Report, Outcome of the public consultation on the draft Scientific Opinion of the EFSA Panel on Contaminants on the Food Chain (CONTAM) on acrylamide in food

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TECHNICAL REPORT

Outcome of the public consultation on the draft Scientific Opinion of the EFSA Panel on Contaminants in the Food Chain (CONTAM) on acrylamide in food[1]

European Food Safety Authority[2, 3]

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ABSTRACT

The EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) has endorsed its draft Scientific Opinion on the risks to public health related to the presence of acrylamide (AA) in food. The opinion has undergone a public consultation from 1 July 2014 to 15 September 2014. Overall, EFSA has received 120 comments from various interested parties including national agencies, academia, industry and individuals in their private capacity. This report summarises the outcome of the public consultation, and lists and provides a brief summary of the comments received and how they were taken into account when finalising the Scientific Opinion for adoption.

KEY WORDS

acrylamide, public consultation, exposure assessment, toxicity, health risks

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SUMMARY

The current report summarises the outcome of the web-based public consultation that was held on the draft Scientific Opinion on the risks to public health related to the presence of acrylamide (AA) in food prepared by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel). The consultation took place from 1 July 2014 to 15 September 2014.

As a result of the consultation, 120 comments were received from 23 different parties, including national agencies and governmental bodies, industry and industry associations, academia and individuals in their private capacity.

This report lists all the comments received, including comments on a specific topic submitted twice by the same organisation but under a different section. It provides a brief summary of the comments and explains how they were addressed by the CONTAM Panel and the opinion revised. The updated version was discussed and adopted by the CONTAM Panel on 30 April 2015 during its 71st Plenary meeting, and published on the EFSA Journal (EFSA CONTAM Panel, 2015).

EFSA thanks all stakeholders for their valuable contributions.

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BACKGROUND AS PROVIDED BY EFSA

In December 2012, the European Commission asked EFSA to for a Scientific Opinion on the risk to human health related to the presence of acrylamide (AA) in food. Considering that the risk assessment was of a sensitive nature and of particular interest to the public and scientific community, it is deemed appropriate to undertake a public consultation on the draft Scientific Opinion before its final adoption by the CONTAM Panel. The public consultation should last at least 6 weeks.

TERMS OF REFERENCE AS PROVIDED BY EFSA

In line with EFSA's policy on openness and transparency, and in order for EFSA to receive comments from the scientific community and stakeholders, EFSA shall release the draft Scientific Opinion on AA in food for public consultation.

Upon completion of the public consultation, a technical report will be prepared aiming at compiling the comments received and at explaining how these will be addressed in the final scientific output.

CONSIDERATION

1. Introduction

The draft Scientific Opinion on the risk to human health related to the presence of acrylamide (AA) in food was prepared and endorsed for public consultation by the EFSA Panel on Contaminants in the Food Chain (CONTAM Panel) on 15 May 2014. The public consultation lasted 10 weeks, from 1 July 2014 until 15 September 2014. This report provides a summary of the written comments received and how they were considered by the CONTAM Panel for revising the opinion.

As a result of the web-based public consultation on the draft opinion on AA in food a total of 194 entries were received. For the sake of completeness, EFSA has also taken into account submissions done by email, even though this was explicitly excluded in the instructions for this public consultation on the EFSA website. Further analysis of the entries showed a number of illegible and empty entries (n = 71) and duplicate submissions by the same organisation (n = 3), which lead to a total of 120 comments. These comments are listed in Appendix A of this report. Comments on a specific topic submitted twice by the same organisation but under a different section were kept for transparency.

The comments were submitted by 23 interested parties including academia, industry and industry associations, national agencies/authorities, other organisations and individuals in their private capacity. Comments submitted formally on behalf of an organisation appear with the name of the affiliation, otherwise they are listed anonymously. The comments are listed in the same language as submitted.

The working group on AA discussed all the comments received and took them into account when revising the draft opinion. Many of the comments received were deemed appropriate and contributed to an enhancement in the scientific quality and clarity of the opinion, and thus the opinion was revised accordingly, providing additional clarifications and explanations. A summary of the main comments received (shown in italics in the next sections) and how they were addressed by the CONTAM Panel is given below. Some comments, especially those suggesting editorial changes, have been directly addressed in the text of the opinion, if they were considered appropriate (EFSA CONTAM Panel, 2015).

The CONTAM Panel would like to thank all the parties for their helpful contributions.

2. General comments

2.1. Comments related to the scope of the draft opinion

Some of the comments suggested the draft opinion should have focus on the evaluation of the mitigation measures and effects in the exposure estimates.

> *In the present situation (after 12 years of broad research), the most useful work of EFSA would be the evaluation of options for mitigation and estimation of their effect on exposure for the concerned groups of consumers* (see comment 9 in Appendix A)

The CONTAM Panel notes that the evaluation of mitigation measures and estimation of their effects on the exposure of the population was not included in the terms of reference for this Scientific Opinion, and were therefore not addressed in the risk assessment. The evaluation of mitigation measures and their effects are, in this specific case, considered to be under the remit of the European Commission.

The EFSA opinion on AA summarizes the current status of potential mitigation measures including the FoodDrinkEurope Toolbox. Where possible, it also describes where mitigation measures resulted

in a decrease of AA levels, such as in the case of various German 'Signalwerte'. However, a European wide evaluation of their effects on dietary exposure is not feasible as respective occurrence data are incomplete and the exposure especially from home prepared food cannot be controlled.

> *Implement state monitoring and supervision over the quality and innocence of the drinking water.: (i) give to the water qualification of product category, (ii) Provide supervision, control and monitoring over producing food, alcohol, nonalcoholic, semi processed goods and carbon dioxide. (iii) Work out the plan for ruling the critical situation, including establishing the crisis ruling group.(iv) Take preventive and coordinating measures considering general principles of food innocence in order avoid risks. (v) Systematically inform population about high risk or harmful food. (vi) Informing population about current issues of food innocence. (vii) Informing producers/distributers and customers about legal demands in the field of innocence food. (viii) Bring to light the facts of falsifications and taking measures* (see comment 6 in Appendix A)

The CONTAM Panel notes that the content of this comment is outside the scope of this risk assessment on AA in food.

2.2. Comments related to initiatives for mitigation measures

A number of comments referred to particular initiatives for mitigation measures, or how the description of initiatives for mitigation measures was done in the draft opinion.

> *The use of asparaginase for acrylamide mitigation has proven successful in a range of food products* (see comments 14, 36 and 114 in Appendix A)

> *The use of acrylamide-preventing yeast technology circumvents the need for a variety of acrylamide control and reduction practice that are logistically and technically challenging, as well as extremely costly* (see comments 39, 40, 104 and 105 in Appendix A)

> *Section 4.5 on 'Initiatives for mitigation measures' should be completed by successful measures which underline that improvements are feasible, such as those in Switzerland with regard to potato products. Use of asparaginase is another successful measure that was not adequately addressed* (see comment 43 in Appendix A)

> *It is important that risk-benefit tradeoffs be considered when considering specific mitigation strategies* (see comment 44 in Appendix A)

As mentioned previously, the CONTAM Panel notes that the evaluation of the mitigation measures was out of the scope of the risk assessment as requested by the EC. In the draft opinion, as well as in the opinion (EFSA CONTAM Panel, 2015), a summary to provide an overview on the initiatives for mitigation measures is given. Moreover, the effects of adding asparaginase before heat processing have now been mentioned.

> *The brochures designed to help food business operators to implement parameters of the toolbox that are relevant for specific sectors are available in 23 European languages.*

> *Industry has contributed to important DG research or national research programmes, such as Heatox and Prometheus as well as a project to control asparagine in wheat. Other efforts concern cooking instructions to help consumers reducing their exposure to acrylamide which is available in 28 languages* (see comments 15 and 42 in Appendix A)

The comment is taken into account and the number of languages in which the brochures are available has been updated to the most recent information up to the date of publication of the opinion in Section 4.5 on 'Initiatives for mitigation measures'. In addition, reference to research activities, such as

HEATOX[4] and Prometheus,[5] were made in Section 4.4 on 'Impact of raw material, storage and processing on AA levels in food' (EFSA CONTAM Panel, 2015).

> *Referring to the description of the Yuan et al. (2014) study, it would appear that the technique as described would be impractical within current commercial settings, and would have some major impacts upon the organoleptic properties of the final foodstuffs. Given this uncertainty we would suggest that the text should be amended to read "The authors believe that optimal soaking treatments could effectively reduce the AA content while reasonably retaining the sensory attributes of the crisps"* (see comment 37 in Appendix A)

The CONTAM Panel notes that the information on the impact of processing provided in Section 4.4.2 on 'Impact on processing' does not aim to be a comprehensive summary and is not meant to be taken as recommendations for possible mitigation measures. In order to clarify this, the Panel has indicated that the experiments described by Yuan et al. (2014) were performed under laboratory conditions (EFSA CONTAM Panel, 2015).

> *Regarding the description of the minimisation measures implemented in Germany it should be added that (i) "The far-reaching successes of the minimisation efforts undertaken in Germany are documented by the continuously lowered signal values (Raters, Matissek 2012), and that (ii) "The effectiveness of the minimisation measures implemented in potato crisp production in Germany since April 2002 is documented by the regularly updated weekly mean values (Raters, Matissek 2012)"* (see comment 45 in Appendix A)

The CONTAM Panel acknowledges the information provided and has added some information on the effectiveness of the minimisation measures implemented in Section 4.5 on 'Initiatives for mitigation measures' (EFSA CONTAM Panel, 2015).

2.3. Comments related to the formation in food, impact of raw material, storage and processing on AA levels in food

A number of comments related to the formation of AA in food and the impact of raw material, storage and processing on the AA levels in food, as follows.

> *It is mentioned that AA-formation starts being relevant at temperatures above 120 °C but no reference is cited to support this. It is not really correct. More important (and hardly ever mentioned) is the absence of water, e.g. crust formation* (see comment 7 in Appendix A)

The CONTAM Panel acknowledges the information provided and has therefore modified the text where appropriate to indicate the relevance of moisture content, e.g. in Section 1.3.3 on 'Formation in food' (EFSA CONTAM Panel, 2015).

> *Ammonium carbonate or ammonium bicarbonate used to raise dough increases the yield of the reaction to AA in bakery ware roughly 10 times. AA formation was substantial at temperatures as low as 80 °C. It was confirmed that the bakery ware and cereals with high AA contents are mostly made with these salts. Ammonium might also contribute to the high AA-formation in potato products. For many products it seems possible to avoid the use of ammonium carbonate, but for others, like gingerbread, it is essential for the product identity* (see comment 18 in Appendix A)

The CONTAM Panel acknowledges the information provided and has therefore modified the text to indicate the specific relevance of ammonium carbonate or bicarbonate, e.g. in Section 4.4.2 on 'Impact of processing' (EFSA CONTAM Panel, 2015).

[4] European Union-funded project 'Heat-Generated Food Toxicants: Identification, Characterization, and Risk Minimization'.

[5] European Union-funded Project 'Process contaminants: mitigation and elimination techniques for high-quality food and their evaluation using sensors and simulation'.

Elimination is neglected in the draft opinion. Elimination may be as determinant for the final AA concentration as formation (which is usually recognized for coffee) (see comment 19 in Appendix A)

The CONTAM Panel acknowledges the information provided and has included in Section 4.4.2 on 'Impact of processing' some information on the formation and reduction of AA levels during coffee roasting (EFSA CONTAM Panel, 2015).

Information is provided on a study to clarify the impact of storage on the formation of acrylamide after frying (see comment 34 in Appendix A)

The CONTAM Panel acknowledges the information provided. However, the Panel notes that a general overview of the impact of potato varieties and storage conditions on the levels of AA is given in Section 4.4.1 on 'Impact of raw material and storage', and does not consider it necessary to add reference to this particular study.

Information is provided on the relevance of frying temperatures and time in the preparation of French fries (see comment 38 in Appendix A)

The CONTAM Panel acknowledges the information provided and has included the results from the study of Fiselier et al. (2006) to reflect on the relevance of the frying temperature in Section 4.4.2 on 'Impact of processing' (EFSA CONTAM Panel, 2015).

2.4. Comments related to the structure, order and clarity of the description of the studies

Some comments related to the structure and order in the description of the studies, and to the overall clarity of the draft opinion, as follows:

The use of AA as an abbreviation for acrylamide seems unnecessary and makes the document harder to read (see comment 1 in Appendix A)

The CONTAM Panel considers that the use of the abbreviation AA to refer to acrylamide in its risk assessment is appropriate.

In the section on hazard identification and characterisation the Panel's conclusions and discussions frequently appear within the body text rather than as a distinct numbered subsection. This format means that it is, in some instances, difficult to read and digest the information that is being presented (see comment 66 in Appendix A)

Most sections of the hazard identification and characterisation chapter contained a distinct separate sub-section named 'conclusions'. In other cases, a concluding paragraph was available but with no distinct sub-section named 'conclusions'. The comment has been taken into account, and the opinion (EFSA CONTAM Panel, 2015) has been modified accordingly to include a distinct section on conclusions for all sub-chapters in the hazard identification and characterisation.

In the reproductive and developmental toxicity section it is recommended to clearly separate the older studies (i.e., those performed before the JECFA assessment in 2005) from the more recent studies. For older studies a short, general description might be sufficient, and the section should concentrate on describing and discussing more recent studies, that are, in fact, those providing more reliable and accurate information (see comments 71 and 78 in Appendix A)

The CONTAM Panel does not agree that as a general rule recent studies are those providing more reliable and accurate information, and for the risk assessment considered all the evidence available. For the purpose of the description of the studies, the Panel summarised those described in previous evaluations briefly, and when necessary made a more detailed description. In the opinion (EFSA

CONTAM Panel, 2015) there has been some reordering of the paragraphs to follow chronological order in the description of the studies.

> *The section on mode of action for endocrine/reproductive toxicity mode of action discusses possible endocrine-related (as well as non-endocrine) mechanisms of reproductive/developmental effects, therefore the title of the section should be reproductive/developmental toxicity. In addition, the section is difficult to follow: what is the rationale of the sequence by which studies are presented and discussed? A more readily understandable sequence would help the reader to agree with the conclusion of the draft opinion* (see comments 81 and 82 in Appendix A)

The CONTAM Panel notes that Section 7.3.6.5 of the draft opinion does not discuss the mode of action for developmental toxicity, but focuses on the mode of action of both thyroid and reproductive toxicity of AA. For the sake of clarity the content has been divided into two sections (7.3.6.5 on 'Mode of action of thyroid toxicity', and 7.3.6.6 on 'Mode of action of reproductive toxicity') to provide a better structure of the studies described (EFSA CONTAM Panel, 2015).

> *With regard to the analysis of epidemiological studies, the report lists all cancers observed in epidemiological studies one after the other. While this approach has the advantage of systematically analysing lines of evidence in response to a specific issue, it can cause the corpus of data and publications to become over-fragmented, ultimately meaning that there is not sufficient perspective to judge a set of arguments that may be a part of a continuum of similar effects* (see comment 91 in Appendix A)

The CONTAM Panel notes that in the draft opinion, besides the description of the cancers studied one after the other, there was a section on 'discussion and conclusions' that considered the epidemiological evidence as a whole. To make this clearer and also according to previous comments, the opinion (EFSA CONTAM Panel, 2015) has been modified to include two distinct sections on (i) considerations on the interpretation of the epidemiological studies and on (ii) the conclusions from the CONTAM Panel.

> *The recommendations made by the CONTAM Panel are very important and should receive greater emphasis within the abstract and within the summary* (see comments 2 and 11 in Appendix A)

The CONTAM Panel notes that the recommendations made were already included in the Summary of the draft opinion. The maximum length of the abstract of the opinion is specified by the EFSA Journal rules, and concentrates on the results of the risk assessment.

> *In Section 1.1 the description of the results of the DTU report on the monitoring of AA in food during the period 2004-2011 may suggest that cocoa has been identified in Denmark to be a major contributor. In the original Danish report it says the contribution from potato products is 'followed by coffee and cocoa at 30 % of which coffee contributes the most, and it is suggested this is indicated in the opinion* (see comment 17 in Appendix A)

The CONTAM Panel has modified the sentence referring to the National Food Institute (Technical University of Denmark) (DTU) report in Section 1.1, to indicate that for adults, the food categories contributing most to the intake were potato products, followed by coffee and cocoa, of which coffee contributed the most (EFSA CONTAM Panel, 2015).

> *In Section 2 it is stated that AA used in food contact materials is restricted by the generic specific migration limit of 60 mg/kg of food. This is wrong: AA must not be detectable in food, whereby the detection limit is 0.01 mg/kg* (see comment 20 in Appendix A)

The CONTAM Panel acknowledges the information provided, and Section 2 on 'Legislation' has been modified to indicate that Commission Regulation (EU) No 10/2011 of 14 January 2011 on plastic

materials and articles intended to come into contact with food stipulates that AA shall not migrate in detectable quantities, whereby a detection limit of 0.01 mg substance per kg food is applicable (EFSA CONTAM Panel, 2015).

> *In Section 4.2 reference is made to the 2012 EFSA monitoring report to state that 'coffee and coffee substitutes' has showed increasing levels during the period from 2007 to 2010. The original report indicates this trend analysis is based on the data for instant coffee only and on a very small data base. The trend analysis is driven by lower than realistic mean levels for 2007 and 2008. In addition, the small 2010 database is influenced by one single outlier with an extraordinary high acrylamide level. Industry data as provided to EFSA does not confirm a trend of increasing levels in instant coffees over time. It is suggested to remove the reference to coffee in the statement* (see comments 32, 33 and 35 in Appendix A)

The CONTAM Panel finds it appropriate to delete the reference to specific food categories when describing the time trend analysis performed in EFSA (2012) due to the limitations in the available data.

2.5. Comments related to missing references

Some comments indicated certain references were not mentioned in the draft risk assessment (comments 66, 87, 96 and 113 in Appendix A). Some of those references, i.e. Luján-Barroso et al. (2014) and Hogervorst et al. (2014), were indeed included and considered in the draft opinion. Others, i.e. Virk-Baker et al. (2014) and Obón-Santacana et al. (2014), were published after 5 May 2014, the cut-off date of the literature review for the draft opinion. Other references indicated were published before the cut-off date, i.e. Mannaa et al. (2006), Clement et al. (2007), Naruszewicz et al. (2009) and Xu et al. (2014). The study by Mannaa et al. (2006) was not cited in the draft opinion since, as indicated in Section 7.3.6.4, only an overview of the publications dealing with the potential protective effects reported for drugs, natural compounds and other chemicals towards biochemical and adverse effects of AA and GA was given in Table H1 (Appendix H) including only studies published from 2010 onwards. For the sake of completeness, Clement et al. (2007) is now included under Section 7.3.6.7. on 'Mode of action of accompanying effects'. For Naruszewicz et al. (2009), the CONTAM Panel noted this was a pilot study but for the sake of completeness has now included the relevant information in Section 7.2.2.2 on 'Use of Hb adducts as biomarkers'. The review by Xu et al. (2014) does not provide original information, but it has been cited in Section 4.4 on 'Impact of raw material, storage and processing on AA levels in food'.

The evidence regarding the hazard identification and characterisation of AA available from the cut-off date of the draft opinion (5 May 2014) until 13 March 2015 has been considered in the final risk assessment (see Appendix B) according to the methodology described in EFSA CONTAM Panel (2015).

3. Specific comments

3.1. Occurrence and exposure sections

Comments were received on the occurrence and exposure sections of the draft opinion. The comments were grouped into categories as follows.

3.1.1. Comments related to the way of reporting the occurrence and exposure data

> *Both in the abstract and the summary product categories with the 'highest levels' are highlighted, but these are not always the products which contribute the largest amounts to dietary intakes. It is important to provide equal emphasis within the abstract and summary to those product categories which have been calculated to contribute significant amounts to dietary intake* (see comments 2 and 11 in Appendix A)

The information provided in the Abstract and Summary of the opinion (EFSA CONTAM Panel, 2015) has been completed to indicate the food category(ies) that was generally the main contributor to the total dietary exposure.

> *The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate as these are independent sub-categories with different levels of AA and which need to be assessed separately* (see comments 2, 3, 5, 8, 11, 13, 29, 101, 103 and 109 in Appendix A)

The CONTAM Panel wants to highlight that the food categories 'Coffee' and 'Coffee substitutes' were treated as separate food categories for the estimation of the exposure in the draft opinion. For the sake of clarity, the Panel agrees to refer separately to the two food groups when presenting the occurrence/exposure data throughout the opinion (EFSA CONTAM Panel, 2015).

> *The comparison of the levels of AA in 'dry' coffee and coffee substitute products (which are not consumed as such) with other products which are ready for consumption may be misleading. Comparison on a semi-finished product basis should be avoided. The comparisons of AA levels in different food categories should be made considering the food (or beverage) 'as consumed'* (see comments 2, 5, 8, 11, 12, 101, 102 and 109 in Appendix A)

The Panel acknowledges that for 'Coffee (dry)' and 'Coffee substitute (dry)' products, the occurrence levels refer to the solid form and not to the diluted form ready for consumption, and in this sense, they cannot be strictly compared to levels observed in most of the other food categories ready for consumption. Almost all occurrence data available for 'Coffee (dry)' and 'Coffee substitute (dry)' were originally expressed on the solid form when submitted to EFSA. In addition, the dilution factor is highly variable depending on the type of coffee beverage consumed (from 0.017 for 'Instant coffee, liquid' to 0.125 for 'Coffee drink, espresso'). The CONTAM Panel consequently decided to keep the description of the occurrence levels expressed on the solid form of the coffee and coffee substitutes products. The text was however revised in order to clearly indicate when it was referring to the solid form or to the diluted (as consumed) form (EFSA CONTAM Panel, 2015).

> *The term 'coffee Americano' is not a common term across Europe. It is proposed to replace the term with 'drip filter coffee'* (see comments 47, 49, 55, 57, 115, 116, 119 and 120 in Appendix A)

The CONTAM Panel notes that 'Coffee drink, café americano' is a standard terminology used in the first version of FoodEx classification (EFSA, 2011). It does not refer to a specific mode of preparation of the coffee, but to coffee drinks of average or weak strength, which are more diluted than the 'Coffee drink, espresso'. The CONTAM Panel decided not to change this standard terminology, but to clearly indicate the definition of 'Coffee drink, café Americano' in a footnote in Section 5.1 on 'EFSA's Comprehensive European Food Consumption Database' (EFSA CONTAM Panel, 2015).

> *Is important to use consistent terminology throughout the draft Scientific Opinion and there should be a clear and consistent differentiation between 'French fries' and 'potato crisps'. Extra care should be taken to clarify whether the reference in the text is to 'Potato Crisps' or to 'Potato Fried Products'* (see comments 24 and 27 in Appendix A)

The CONTAM Panel notes that in Sections 4, 5 and 6 the terminology 'Potato crisps' was consistently referring to crunchy thin slices of deep-fried/baked potato usually eaten as snacks, whereas 'French fries' was referring to batons of deep-fried potato usually served as an accompaniment during a meal. This was defined in Section 4.1.2.3 on 'Food description'. In other sections of the draft opinion that cited studies from the literature (e.g. Section 6.3 on 'Previously reported human exposure assessments'), the original food name provided by the authors was used. In those sections, and in order to avoid misinterpretations, the name of the product according to the definitions above has now been specified in brackets, when possible. In addition, besides the paragraph in Section 4.1.2.3, an additional paragraph is now added at the beginning of the Scientific Opinion (Section 1 on 'Introduction') to clarify the terminology used (EFSA CONTAM Panel, 2015).

For clarity it is suggested that where 'Potato Fried Products' are referenced as a standalone category, they should be referenced as 'Potato Fried Products (except potato crisps and snacks)' (see comments 24 and 27 in Appendix A)

Although it was already clearly stated in the opinion that the term 'Potato fried products' referred to potato fried products other than potato crisps and snacks, in order to increase clarity, the CONTAM Panel now used the term 'Potato fried products (except potato crisps and snacks)' (EFSA CONTAM Panel, 2015).

The occurrence data of food category 6.4 (Gingerbread and Lebkuchen) are used for speculaas in the baseline exposure scenario. This does not correspond to the real occurrence data for speculaas since 2010. It is more appropriate to use the occurrence data of food category 6.3 (Biscuits and wafers). Speculaas is a biscuit and the composition and processing are not comparable to the composition of gingerbread or lebkuchen (see comment 58 in Appendix A)

The CONTAM Panel acknowledges the information provided although noted it refers only to a few samples analysed with mean values ranging from < 200 to 346 µg/kg. Only this information and the limited number of samples submitted to EFSA for speculoos, did not allow moving speculoos from category 6.4, used by most of the data providers, to 6.3 as suggested. Moreover, the Panel notes that there were uncertainties in the reported data to EFSA by the data providers regarding the classification of products, such as speculoos. Due to the limited number of eating occasions for this latter food commodity across countries and age groups as reported in the European Comprehensive Food Consumption Database, this is expected to have a negligible impact on the exposure estimates.

The calculations performed in Section 6.2.3 do not appear to be about loyalty to a particular brand, but loyalty to a particular product category. It is suggested that the title of this section needs to more closely reflect the calculations that have been undertaken, e.g. Loyalty to particular product sub-type or category (see comment 64 in Appendix A)

The CONTAM Panel acknowledges that the terminology 'brand loyalty' in this context is not adequate since the exposure scenarios in this section reflect the loyalty to certain type of products rather than to a specific brand. The term 'brand loyalty' is now replaced by 'preference for particular products' (EFSA CONTAM Panel, 2015).

3.1.2. Comments related to the comparison of AA levels between food groups

Some comments received referred to the limitations when comparing the AA levels observed in different types of coffee.

It is stated that 'roasted coffee' was found to be less contaminated than 'instant coffee' on basis of the analysis of the 'dry (as sold)' products. This is less relevant than the comparison of the levels in the products 'as prepared for consumption', where both sub-categories are at a similar level (see comments 28, 30, 101 and 110 in Appendix A)

The CONTAM Panel notes that it is indeed important to highlight that the difference in occurrence observed when comparing coffee products on dry matter may be minimized when considering the different dilution factors for the respective coffee beverages. A sentence has been added to Section 4.1.3.6 on 'Coffee (dry)' (EFSA CONTAM Panel, 2015).

The comparison between 'regular' and 'decaffeinated' coffee is based on monitoring data and the regular and decaf subsets are not comparable due to different blends and roasting conditions. It is proposed to refer to the conclusion on the effect of decaffeination as included in the FoodDrinkEurope Toolbox (see comments 28 and 31 in Appendix A)

The CONTAM Panel notes that the comparison between the AA levels in regular and decaffeinated coffee as in the draft opinion is based on the observations of the occurrence data. The results should be

interpreted with caution due to the different numbers of samples, brands and roasting conditions. This is now indicated in the opinion. A reference to literature data showing the absence of decrease of AA level during the decaffeinating (Andrzejewski et al., 2004) has also been included in Section 4.1.3.6 (EFSA CONTAM Panel, 2015).

3.1.3. Comments related to the assumptions made for the exposure modelling

It is recommended that EFSA reconsider whether 5% is the proper cut-off for assuming the potato was fried in consumer surveys (see comment 48 in Appendix A)

In the exposure assessment, in the absence of any clear indication on the mode of preparation of the potatoes in the consumption surveys, it was assumed that if more than 5 % oil/fat was consumed during the same meal, then the potato was classified as 'French fries and potato fried'. The CONTAM Panel acknowledges that some French fries can contain more than 10 % oil/fat, and that some non-fried potato products can contain more than 5 % oil/fat. However, in this assessment, the food group 'French fries and potato fried' did not include only 'French fries', but also 'Potato fried', 'Potato croquette' and 'Roasted potato'. Some commercial products of 'Potato croquette' and 'Roasted potato' available on the European market are indicated to contain oil/fat at levels close to 5 %. In order to not underestimate the exposure levels of the European population, the cut-off value was consequently set at 5 %. The rationale for the selection of 5 % as cut-off value is reflected in Section 5.1 on 'EFSA's Comprehensive European Food Consumption Database' (EFSA CONTAM Panel, 2015).

In order to quantify the uncertainties introduced by such an assumption, two extreme scenarios were considered. The first one assumed all the unspecified consumption events of potatoes as 'French fries and potato fried', and the other considered all the unspecified consumption events of potatoes as 'Non fried potato products' (for details see Section 6.2.4 on 'Considerations on unspecified and/or raw potato products' (EFSA CONTAM Panel, 2015)).

The dilution factor used to recalculate from coffee substitutes (solids) to coffee substitutes (beverage) is not in accordance with actual market practice and advice for product preparation. The dilution factor should be 0.02 (see comments 56, 57, 118 and 120 in Appendix A)

The CONTAM Panel acknowledges that according to actual market practice and advice for product preparation, a dilution factor of 0.02 applies to 'as sold' soluble coffee substitute products and in the same magnitude as the dilution factor for drip filter coffee (around 0.05) to 'as sold' roast and ground coffee substitute products. In addition, and after further investigations, the CONTAM Panel notes that the dilution factor of 0.125 used for 'Coffee drink, espresso' was not in line with actual advices for product preparation.

The CONTAM Panel has now updated the exposure assessment considering the dilution factors in Table 1. Regarding coffee substitutes beverages, in the absence of a distinction between those made from soluble coffee substitutes and those made of roasted coffee substitutes, the CONTAM Panel used the highest dilution factor of 0.05 in the calculations. The Panel highlights that the use of the updated dilution factors did not change the overall exposure estimates.

Table 1: Dilutions factors used in the draft opinion and updated dilutions factors used in EFSA CONTAM Panel (2015)

Coffee and coffee substitutes beverage	Dilution factors used in the draft opinion (EFSA CONTAM Panel, 2014)	Dilution factors used in the opinion (EFSA CONTAM Panel, 2015)
Coffee drink, espresso	0.125	0.20
Coffee drink, café américano	0.053	0.05
Coffee drink, cappuccino	0.044	0.05
Coffee drink, macchiato	0.063	0.10
Iced coffee	0.035	0.04
Coffee with milk	0.035	0.04
Instant coffee, liquid	0.017	0.02
Coffee substitute beverage	0.125	0.05

For the exposure estimation to AA only the Lower Bound and the Upper Bound approach are used. Why not the Medium Bound (MB)? (see comment 62 in Appendix A)

The CONTAM Panel did not consider necessary to report medium bound (MB) exposure estimates since the estimates under the lower bound (LB) and upper bound (UB) scenarios were very close. The small range between the LB and UB exposure estimates is mainly due to the overall low number of left-censored data, and to the assumption used for both the LB and UB scenarios for the treatment of results below the limit of detection (LOD)/limit of quantification (LOQ) for the food and food groups with less than 60 % of left-censored results. Mean occurrence values used for the assessment of the LB and UB dietary exposure to AA were estimated as follows (see WHO/IPCS, 2009; EFSA, 2010):

- In the LB exposure scenario, for food and food groups with more than 60 % of left-censored results, the occurrence values below the LOD/LOQ were set at 0, while for food and food groups with less than 60 % of left-censored results, occurrence values below the LOD/LOQ were set at half the LOD/LOQ.

- In the UB exposure scenario, for food and food groups with more than 60 % of left-censored results, occurrence values below the LOD/LOQ were set at the LOD/LOQ, while for food and food groups with less than 60 % of left-censored results, occurrence values below the LOD/LOQ were set at half the LOD/LOQ.

In order to add clarity, the description of the methodology has been revised in Section 6.1.2 on 'Exposure calculation' and in Appendix D (EFSA CONTAM Panel, 2015).

Regarding the left-censored management, why does EFSA refer to the WHO guidelines (GEMS/Food-EURO, 1995) and not to the Guidance of the EFSA Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment (2006)? (see comment 59 in Appendix A)

The references to the guidelines for left-censorship management have now been updated to refer to World Health Organisation (WHO)/International Program on Chemical Safety (IPCS) (WHO/IPCS, 2009) and EFSA (2010). The CONTAM Panel notes that these references are based on the WHO Guidelines (GEMS/Food-EURO, 1995).

3.1.4. Comments related to the description of the exposure assessment and its methodology

In Section 6.1.2 on 'Exposure calculation' it is suggested to modify the sentence describing how the chronic exposure was estimated (see comment 60 in Appendix A)

The comment suggested to modify the following sentence: '*Chronic exposure to AA was assessed at the individual level by multiplying the mean daily consumption for each food with the corresponding mean contamination, summing up the respective intakes throughout the diet, and finally dividing the results by the individual's body weight'* by *'Chronic exposure to AA was assessed at the individual level by multiplying the mean daily consumption for each food with the corresponding mean contamination, **resulting in a distribution of exposure**, summing up the respective intakes throughout the diet, and finally dividing the results by the individual's body weight'*. The CONTAM Panel considers the suggested modification not appropriate since this sentence describes how the exposure is assessed at the individual level. At the individual level, the calculation is done in a deterministic manner, i.e. resulting in a single intake estimate by food, and then a single exposure estimate by individual, and not in a distribution of exposure. However, at the population level the method leads to a distribution of individual exposure levels. Therefore, the following sentence was revised in Section 6.1.2 of the opinion (EFSA CONTAM Panel, 2015): *'This resulted in a distribution of individual exposures from which the mean as well as the 95th percentile were derived for each population group (i.e. [survey and age group] combinations)'*.

The exposure estimates in Table 8 appear very similar and it is not possible to determine if the levels are really different. Is it possible to comment on the uncertainties around the means? (see comment 61 in Appendix A)

Table 8 in Section 6.2.1 'AA exposure levels across the different population groups' presents the minimum, median and maximum of the mean and 95th percentile exposure levels across the different surveys and age groups. The CONTAM Panel highlights that in order to estimate the exposure, a single 'European' mean occurrence level for each food item was used without taking into account possible variability between countries. Since AA is found in a number of commonly consumed foods, this can explain why the exposure estimates across surveys of the same age class do not differ considerably.

In section 6.2.2.the food groups contributing to the AA exposure are reported. However, this is an incomplete and selective summary, making it difficult to read. It would be very useful to provide a full report of the actual percentage contributions to exposure for each food group and each population category (see comment 63 in Appendix A)

The CONTAM Panel notes that the detailed information on the percentage of contribution of the food groups considered in the exposure estimates was given in Appendix F. The Panel finds it appropriate that only a summary of the most relevant findings is given in the main body of text (Section 6.2.2), where the reader is referred to Appendix F for more detailed information.

The use of the scenario modelling is appropriate but the base-line scenario is not sufficiently explained (see comment 54 in Appendix A)

The text in Section 6.1.3 on 'Exposure scenarios' has now been revised and a specific paragraph has been added to explain the baseline exposure scenario (EFSA CONTAM Panel, 2015).

Exposure estimates should go into two directions: (i) population-oriented estimates (as presented in the draft opinion) to conclude that the margin of exposure (MOE) indicates a concern; (ii) exposure modeled by scenarios of consumer habits (combinations of food consumption with estimated AA-concentrations). Scenarios enable the detection of extreme exposures that are missed by statistical approaches. In the present draft the modeling approach is not even addressed, even though important additional conclusions could be drawn – in particular it must

be assumed that for some consumers exposure is markedly higher than now assessed (see comment 53 in Appendix A)

Exposure assessments tend to underestimate home-made foods. It is questionable that the samples of "other potato fried products" reflect the full spectrum of products. This might explain the poor correlation between the estimated dietary exposure and internal biological markers (see comment 26 in Appendix A)

The comments suggest that the population-oriented estimates were not enough to detect extreme exposures, and mention the pertinence of modelling exposure through scenarios reflecting specific consumption behaviours. The CONTAM Panel considers such approach was implemented in the draft risk assessment, where a number of scenarios were designed in order to assess the impact of specific consumption habits on the exposure levels that were not reflected in the baseline exposure scenario. Such scenarios revealed that depending on consumers' habits regarding the potato fried products, the exposure levels could be from 22 % lower and up to 80 % higher, than those estimated in the baseline exposure scenario. Consumer's habits or preferences towards other types of products (potato crisps, coffee beverage and toasted bread) resulted in more limited variations of the exposure levels. Even higher exposure may occur especially given the variability in home-cooking practices and individual consumption preferences.

3.1.5. Comments related to the category 'Coffee beverages'

It would be interesting to have more details on the data for 'Unspecified coffee (Beverage)' since this covers a significant number of samples (see comments 117 and 120 in Appendix A)

A detailed analysis of the EFSA Comprehensive European Food Consumption Database has been performed in collaboration with the data providers, in order to identify and correct some misclassification of coffee and coffee substitutes products (e.g. coffee powder codified as coffee beverage and vice versa) and also to describe more precisely the coffee beverage which were classified as 'Unspecified coffee beverages'. The exposure assessment has now been updated according to these corrections (EFSA CONTAM Panel, 2015).

In addition, the assumption made on the remaining 'Unspecified coffee beverages' was revised. The average portion sizes (consumption level by occasion of consumption) of 'Unspecified coffee beverages' estimated across the surveys in the adults, elderly and very elderly age groups ranged from 103 to 332 mL. According to actual market practices and advices for product preparation, a 'Coffee drink, espresso' is 30–50 mL, whereas the other coffee beverages are in the range of 100–250 mL. Therefore, the exposure assessment has been updated assuming that the 'Unspecified coffee beverages' corresponded to beverages which are more diluted than 'Coffee drink, espresso' (see Section 5.1 on 'EFSA's Comprehensive European Food Consumption Database' of EFSA CONTAM Panel, 2015).

3.1.6. Other updates performed in the exposure assessment

Information from six new consumption surveys made available to EFSA after the endorsement of the draft opinion for public consultation has been considered and the exposure estimates updated accordingly. These new consumption surveys included two surveys on specific population groups (i.e. pregnant women and lactating women) (see Section 5.1 of EFSA CONTAM Panel, 2015).

3.1.7. Comments related to the non-dietary exposure

Some comments related to the non-dietary sources of AA exposure and their consideration on the overall assessment as follows.

The section on 'Potential non-dietary sources of exposure' could be expanded, and should include quantitative data on other sources wherever possible (or note when this is not possible) which would allow for a better understanding of the contribution of dietary exposure and would

aid in interpreting the epidemiological studies and risk characterisation. This particularly relates to quantification of acrylamide exposures in smokers and also from environmental tobacco smoke. Data from studies that have measured haemoglobin adducts as an index of internal dose may be particularly helpful in this regard, but other analytical approaches could also be useful (e.g. estimation of inhaled doses, given measured concentrations in the air of workplaces) (see comment 65 in Appendix A)

The Risk Characterisation should be expanded to consider the context of other sources of exposure (see comment 60 in Appendix A)

It is recommended that a detailed analysis be made of kinetic differences between the inhalation and oral routes in humans, and also between human and animal exposures to investigate further the differences in susceptibility to tumours between species and following different routes of exposure (see comment 68 in Appendix A)

According to the terms of reference as provided by the European Commission, the risk assessment should address the human health risks related to the presence of AA in food and thus does not focus on other sources of exposure. The CONTAM Panel however considered the exposure to AA sources other than the diet in Section 6.4 of the draft opinion on 'Potential non-dietary sources of exposure'. This section summarises the main aspects in relation to sources of exposure other than the diet, e.g. occupational exposure and smoking. More detailed data on the comparison of the levels of AA adducts in occupationally exposed populations, smokers and non-smokers have been now added (EFSA CONTAM Panel, 2015). The Panel notes that pharmacokinetic measurements or Physiologically Based PharmacoKinetic (PBPK) modelling exercises to evaluate the kinetic differences between oral and inhalation routes in humans or experimental animals are currently not available.

3.2. Toxicokinetics of AA

Some written comments were received on the toxicokinetics of AA as follows:

To what extent is AA metabolised by conjugation with glutathione and to what extent by epoxidation to glycidamide? Do you have information about this? If yes, could this information be implemented into the opinion? (see comment 4 in Appendix A)

The description of the metabolic pathways of AA in animals and humans were described in the draft opinion in Section 7.1.2 on 'Metabolism', including the available information on the extent of metabolism by conjugation with glutathione and by epoxidation to glycidamide (GA).

In the description of the NTP study on GA it is not clear the correspondence between the GA dose level and the AA intake that may produce that internal GA exposure (see comment 73 in Appendix A)

The NTP rodent bioassays were conducted using equimolar concentrations of AA and GA in the drinking water to facilitate direct comparisons and this has now been indicated in Section 7.3.2.1 (EFSA CONTAM Panel, 2015). The CONTAM Panel noted that both mice and rats convert a substantial fraction of the administered AA dose to GA, based on serum area under the curve (AUC) values (Table 17 of EFSA CONTAM Panel, 2015). It is likely that this efficient metabolism to GA contributed to the similar tumour sites observed in mice and rats from either AA (see Tables 23 and 24, respectively) or GA dosing (Sections 7.3.4.1 and 7.3.4.2, respectively). The metabolic differences between species were explained in detail in Section 7.1.5.1 since the PBPK modelling results allow inter-species comparisons to be made. Based on the remarkably similar tumour incidences between AA- and GA-dosed rats and mice, the role for GA in genotoxicity is clear. However, since reproductive toxicity endpoints in AA-dosed rodents result from combined internal exposures to AA and GA, it is difficult to attribute quantitatively the contribution of each given that both AA and GA are reactive toward different target macromolecules, i.e. AA with proteins versus GA with DNA bases and proteins (see Section 7.3.6.6. on 'Mode of action of reproductive toxicity').

Greater consideration could be given to potential impact of CYP2E1 being polymorphic in humans, highly inducible by alcohol, and expressed in Clara cells (see comment 68 in Appendix A)

The role of CYP2E1 in the metabolism of AA was extensively covered in the draft opinion, including the importance of alcohol consumption and polymorphism in humans. The CONTAM Panel notes that as no new publications on this subject are available, any further consideration would be speculation. The role of Clara cells, which only occur in lung (bronchiolar exocrine cells, more recently termed 'club cells'), are not considered of relevance for the oral exposure to AA.

It is suggested to complete the description of the studies in Section 7.1.1 on placental transfer with the outcomes from the study by Pedersen et al. (2012) (see comment 69 in Appendix A)

The CONTAM Panel considered the additions of relevance to provide a comprehensive description of the outcomes of the studies and has therefore included the information in Section 7.1.1 on 'Absorption and distribution' (EFSA CONTAM Panel, 2015).

3.3. Comments related to biomarkers of exposure/effect

It is suggested to complete the description of the studies cited in Section 7.2.2.2. on 'Hb adducts' with the outcomes of the study by Pedersen et al. (2012) (see comment 69 in Appendix A)

The CONTAM Panel considered the additions of relevance to provide a comprehensive description of the outcomes of the studies and has therefore included the information in Section 7.2.2.2 of EFSA CONTAM Panel (2015). There is further description of the study of Pedersen et al. (2012) in Section 7.4.2.1 on 'Epidemiological studies: pre-natal exposure'.

It is suggested to complete the information on the description of the study by Hochstenbach et al. (2012) regarding the correlations between AA-Hb and micronuclei and GA-Hb and micronuclei in cord blood of 45 male newborns (see comment 113 in Appendix A)

The CONTAM Panel has included now a description of this aspect of the study of Hochstenbach et al. (2012) in Section 7.2.4. Other aspects of this study are described in Section 7.4.2.2 (EFSA CONTAM Panel, 2015).

3.4. Repeated dose toxicity of AA in experimental animals

Some comments discussed the appropriateness of using the Harderian gland as reference point for the derivation of a $BMDL_{10}$ value.

The Harderian gland is an appropriate tumour to use for the BMDL derivations. Whilst not present in humans, it was well established that tumours in this gland were typically associated with genotoxic carcinogens and therefore it was difficult to exclude them from an assessment of carcinogenic potential (see comment 70 in Appendix A)

As humans do not have Harderian gland, the relevance of using this endpoint to translate carcinogenic potential to humans is highly suspect. It seems more appropriate to use the BMDL10 values based on rodent mesothelioma or sarcomas models listed in Table 28 to develop MOE. It is recommended that EFSA reconsider whether the risk assessment should be based on the BMDL10 value derived from the Harderian gland of rodent (see comment 67 in Appendix A)

The CONTAM Panel considered that even though the Harderian gland is not present in humans, this rodent organ represents a sensitive endpoint for detecting compounds that are both genotoxic and carcinogenic, as reasoned in Section 7.5.2 of the draft opinion and in EFSA CONTAM Panel (2015). The Panel concluded that the results on the Harderian gland in mice cannot be disregarded in the risk

assessment of AA, and also noted it provided the lowest $BMDL_{10}$ of the accepted models (see Table 28 and Appendix K of the draft opinion and EFSA CONTAM Panel, 2015).

3.5. Reproductive and developmental toxicity

A remarkable gap is the lack of an up-to-date extended one-generation or two-generation study in order to assess the effects on reproductive development and maturation upon pre- and post-natal continuous exposure. This should be noted in the Opinion (see comment 72 in Appendix A)

The CONTAM Panel agrees with this comment and has now mentioned in Section 7.3.5.1 that, besides the Tyl et al. (2000) study, no other one- or two-generation studies investigating the effects of AA on reproduction upon pre- and post-natal continuous exposure could be identified.

It is surprisingly that dose-related degeneration of the testicular germinal epithelium is questioned as adverse effect, as it is a pathologic alteration. It is long-time established knowledge that the rodent spermatogenesis has a much greater functional reserve than the human one. Therefore, an appropriate non-observed-adverse-effect level (NOAEL) for male reproductive toxicity should consider the histopathology of testis (and accessory glands) and sperm parameters as potentially human-relevant endpoints, even in the absence of an appreciable decrease of male reproductive performance which might remain undetected in rodent standard studies. It is also questionable the relevance of the comment that this lesion was not observed in two old (Johnson et al., 1986; Friedman et al., 1995) and two recent (NTP, 2012, 2013) 2-year studies. Testicular lesions in such studies can easily be obscured by aging-related changes, whereas this does not occur in repeated-dose toxicity studies using young adult animals. Thus, the NOAEL for male reproductive toxicity could be reconsidered, with a strong focus on the studies performed after 2005 and assessing testicular histology and sperm parameters (see comment 74 in Appendix A)

The Panel should consider to establish a NOAEL (or BMD10) for the endpoint "histopathological alterations of the male reproductive tissues" (see comment 76 in Appendix A)

The CONTAM Panel emphasises that the effects on the testicular germinal epithelium were not disregarded. In several repeated toxicity studies in rats and mice, degeneration of the testicular germinal epithelium was observed. In some studies, effects were observed at the lowest dose tested 5 mg/kg b.w. per day, however, overall, the lowest NOAEL for this effect was 2.1 mg/kg b.w. per day in a 90-day drinking water study in rats (NTP, 2012). Regarding the 90-day AA dietary study, the CONTAM Panel concluded that there was too much uncertainty about the biological relevance of the findings to be used to establish a reference point for use in the risk characterisation. The Panel noted that treatment-related changes in the testicular germ cell epithelium were not observed in the 2-year studies (Beland F, 2015, personal communication). This has now been made clearer in the opinion (EFSA CONTAM Panel, 2015). The CONTAM Panel therefore considered the NOAEL of approximately 2 mg/kg b.w. per day as the relevant one for reproductive toxicity.

The Panel should consider to establish a NOAEL for the endpoint "persistent structural changes in the developing brain" (e.g., Ogawa et al., 2011). Such NOAEL might be the basis to determine an overall NOAEL for developmental effects of acrylamide (see comment 77 in Appendix A)

The current conclusions drawn on the study by Ogawa et al. (2012) are not clear: there is an irreversible structural change in a brain region and this is not considered adverse? As it is expressed, this seems inconsistent with the rest of the draft opinion: AA is a recognized neurotoxicant and a potential developmental toxicants, so the overall evidence may allow to assess the biological relevance of early, but persistent, brain structural changes observed in one developmental study. The possible relevance of the study by Ogawa et al. in the definition of a developmental NOAEL could be reconsidered (see comment 80 in Appendix A)

The CONTAM Panel considers that the biological significance of the findings described by Ogawa et al. (2012) needs to be established (e.g. in relation to behavioural alterations) before these data can be used for the establishment of a NOAEL. It also noted that peripheral nerve (sciatic) axonal degeneration is a structural change which is clearly adverse. In addition, the CONTAM Panel noted that the methodology used for counting cells in Ogawa et al. (2011, 2012) does not comply with the principle of stereology, which is the best-practice method for quantitative histology to accurately quantify the number of cells. Even if the findings reported are of potential interest, they need to be confirmed by suitable methodological approaches before being used for establishing a reference point. This has been now clarified in Section 7.3.5.2 on 'Developmental toxicity' (EFSA CONTAM Panel, 2015).

3.6. Epidemiological studies on AA

Comments were received on the description and evaluation of the epidemiological evidence as follows.

3.6.1. Comments related to occupational studies and cancer

> *EFSA had concluded that epidemiological studies of occupational exposure to acrylamide did not indicate an increased risk of cancer whereas earlier authors had judged that the evidence was suggestive of a risk (Siemiatycki et al., 2004; Bagga et al., 2012)* (see comment 85 in Appendix A)

The CONTAM Panel noted that the Siemiatycki et al. (2004) review did not include the 2007 follow-up publications of the two occupational cohorts available to date. In the extended follow-up of the occupational cohorts the association between AA exposure and pancreatic cancer was weaker and not consistent with a dose-response relationship. The report of Bagga et al. (2012) used the conclusion from Siemiatycki et al. (2004) to assume that AA is causally related to the risk of pancreatic cancer and calculated the fraction of pancreatic cancer cases in the UK attributed to occupational exposure to AA. The Panel noted that the calculation was based on the risk estimate for a high exposure group and that was not statistically significant. The estimate was thus derived from an analysis that did not show a consistent dose-response relationship and that was not adjusted for confounding by cigarette smoking. The opinion (EFSA CONTAM Panel, 2015) includes now the Siemiatycki et al. (2004) review, but the Panel does not find it appropriate to refer to the Bagga et al. (2012) study since the results are not an original research study on the association between AA exposure and cancer risk. Because of the results from the extended follow-up, the CONTAM Panel stands by the previous conclusions.

3.6.2. Comments related to the dietary studies and cancer

A number of comments related to the epidemiological studies on the association between AA and human cancer risk.

> *There is no conclusive scientific evidence that support a relationship between dietary acrylamide intakes and increased risk of cancer. EFSA references Lipworth et al., 2012 to support its position in the scientific opinion that the current review papers did not provide a quantification of cancer risk. It is recommended to incorporate the entire conclusion of Lipworth et al. (2012) ["we found no consistent or credible evidence that dietary acrylamide increases the risk of any type of cancer in humans… In particular, the collective evidence suggests that a high level of dietary acrylamide intake is not a risk factor for breast, endometrial, or ovarian cancers… In conclusion, epidemiological studies of dietary acrylamide intake have failed to demonstrate an increased risk of cancer…]"* (see comment 67 in Appendix A)

The CONTAM Panel notes that the review by Lipworth et al. (2012), as well as other reviews, were mentioned in Section 7.4.1.2.6 and these reviews concluded that there was no association between dietary AA exposure and the risk of most common cancers (EFSA CONTAM Panel, 2015). The

CONTAM Panel conclusions were based on all the available evidence from original research studies and meta-analyses.

> *It is suggested that the risk assessment clearly outlines the perspectives as per how unequivocal and clear results from animal toxicological studies should be interpreted in a situation where human epidemiological studies are equivocal* (see comment 91 in Appendix A)

The CONTAM Panel considers that in the absence of clear epidemiological evidence, the risk assessment should be based on data from studies in experimental animals, unless there is clear evidence that the findings in experimental animals are not relevant to humans. This principle has been followed in the CONTAM Panel risk assessment of AA in food.

> *It is suggested that the risk assessment clearly describes and outlines how the statistical power of human epidemiological studies can and should be included in the evaluation of the epidemiological evidence* (see comment 91 in Appendix A)

The CONTAM Panel agrees that the lack of statistical power of many epidemiological studies should be discussed in the evaluation of the epidemiological evidence. Therefore, the Panel has introduced this issue in the Scientific Opinion in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies', as well as in the final 'Recommendations' indicating that the limited size of certain studies (or subgroups within), the low incidence of specific cancers, as well as a potential misclassification of AA exposure, has likely decreased the statistical power of the epidemiological studies. This is especially relevant if possible small effects are to be detected and the variation of exposure is relatively small. Furthermore, measurement error of potential confounders, like energy intake and smoking, may have additionally contributed to the limited statistical power.

> *The focus is largely on the marginal impact of relatively small and imperfectly measured variations in dietary intake, with smoking (including the additional exposure to acrylamide that it entails) treated as a potential confounding variable. However, such marginal effects are not directly relevant to the assessment of exposure-response, especially if smoking contributes more than diet to internal dose. While presentation of results stratified by smoking is helpful in this regard, it would be valuable also to consider the human evidence on risks in relation to total exposure to acrylamide from all sources. The studies that have examined risk of cancer in relation to haemoglobin adducts do this. However, the adduct levels are not necessarily representative of long term exposure* (see comment 83 in Appendix A)

The CONTAM Panel notes that in the opinion special attention is given to the analyses that are restricted to non- or never-smokers. Because cigarette smoking is the most important environmental risk factor for cancer, confounding by smoking needs to be addressed accurately. Furthermore, cigarette smoking is an important source of AA, and smokers have considerably higher levels of AA-Hb adducts than non-smokers (see Section 7.2.2.2 of EFSA CONTAM Panel, 2015). Thus, smoking may bias (or obscure) the association between AA through diet and cancer risk. For this reason, restriction to never-smokers is the most thorough way to control possible confounding by smoking.

Some studies used biomarkers (AA- or GA-Hb adducts) to measure AA exposure. In these biomarker studies, Hb adduct levels for AA and GA reflect exposure through all sources (e.g. diet, smoking, occupation, etc). These biomarker studies have been discussed in the Scientific Opinion and have been summarised in Section 7.4.1.2.7. Cigarette smoke contains thousands of carcinogens and bioactive substances. These carcinogens and substances might further increase (or sometimes decrease) the risk of cancer. Therefore, also in analyses of studies that used biomarkers, (residual) confounding by cigarette smoking could obscure outcomes.

> *When evaluating the studies of occupational exposures, results should be set in the context of estimated internal doses as compared with those from dietary sources in the general population.*

It would be helpful to know whether they are likely to have been similar in magnitude or orders of magnitude higher (see comment 83 in Appendix A)

The CONTAM Panel notes that internal exposures to AA from the diet, smoking and occupational exposure were already compared and discussed in Section 7.4.1.2.7 of the draft opinion. The internal AA exposures in occupationally exposed workers have been reported to be considerably higher (especially in the past) than internal AA exposure from diet. It should furthermore be noted that, compared to exposure from diet, occupational exposures are highly variable and relatively limited in time, they generally include only men and are thus not able to analyse possible risk of certain cancers such as endometrial and ovarian cancer, and participants in the cohorts tend to be healthier than the general population (also known as the 'healthy-worker effect').

Another consideration should be the risk of relevant health outcomes in relation to smoking – about which there will often be quite a lot of information. Tobacco smoke contains many other toxic substances as well as acrylamide, but it seems unlikely that its other constituents would importantly protect against adverse effects of acrylamide. Thus, if smoking has a major impact on personal exposures to acrylamide, and there is good evidence that a health outcome is not importantly related to smoking, then it is reasonable to suggest that outcome is probably not caused by acrylamide. Such consideration might be relevant, for example, to colon and thyroid cancer (see comment 83 in Appendix A)

The CONTAM Panel notes that there are two cancer sites for which there is now ample epidemiological evidence that cigarette smoking is associated with a decreased risk of that cancer. Tobacco smoking has been consistently associated with a decreased risk of post-menopausal endometrial cancer (Cook et al., 2006). Smoking is not associated with ovarian cancer overall, but a large collaborative analysis including almost all available epidemiological studies showed that smoking is associated with an increased risk of the mucinous subtype, and a decreased risk of the endometrioid and clear-cell subtypes (Collaborative Group on Epidemiological Studies of Ovarian Cancer, 2012). The absence of an association between smoking and an increased risk of cancer, does therefore not eliminate the possibility that AA is associated with an increased risk of (subtypes of) a specific cancer. This is now discussed in Section 7.4.1.2.7 of the opinion (EFSA CONTAM Panel, 2015).

More specifically, the comment suggests using this argument for colon and thyroid cancer. Although relative risks are small, cigarette smoking is positively associated with risk of colorectal cancer, as has been shown by a recent meta-analysis (Cheng et al., 2015). Other studies have shown that cigarette smoking might be inversely associated with the risk of thyroid cancer (e.g. Kitahara et al., 2012). The assumption that cigarette smoking is not associated with colon and thyroid cancer is not substantiated by the literature.

The review carefully presents information about stratification by smoking and results on non-smokers – it may help to state that conclusions would be similar if considering results in non-smokers or results from (the small number of studies) with information on adducts (see comment 83 in Appendix A)

The CONTAM Panel notes that results regarding the association between AA and cancer risk as measured through biomarkers or questionnaires are not consistent. For example, most questionnaire studies did not show an association between AA and risk of breast cancer, while the two publications that measured AA and GA adducts did show an increased risk of oestrogen-receptor-positive breast cancer and a decreased breast cancer survival, respectively (Olesen et al., 2008; Olsen et al., 2012). This was discussed in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' (EFSA CONTAM Panel, 2015).

In the opinion, results of dietary AA intake and cancer risk in non- or never-smokers have been discussed and compared to the results in all subjects. The CONTAM Panel notes that the statement

made in the comment that results are similar in all subjects and in non-smokers only, is not completely true for all cancer sites. For example, the meta-analysis from Pelucchi et al. (2015) showed that associations of dietary AA intake are stronger in non-smokers than in all subjects.

> *The epidemiological studies are predominantly based on Food Frequency Questionnaire (FFQ) data. Such data are not very reliable, and the limitations should be explained better in the relevant discussion section. In particular, a number of studies provided some validation information and this could be discussed further e.g. correlation coefficients comparing FFQ estimated intakes with those from food diaries and with measured adducts in Hb* (see comment 86 in Appendix A)

The CONTAM Panel considers it appropriate to further discuss the limitations of the FFQs used to assess AA intake, as well as the comparison of AA estimates from FFQ and those from Hb adducts. To make them more visible, they are now in a separate subsection, i.e. Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' (EFSA CONTAM Panel, 2015). Further description of some of these studies is in Section 7.2.2.2 of the opinion on 'Use of Hb adducts as biomarkers'.

> *In relation to the case-control studies, some discussion around possible biases should be included* (see comment 86 in Appendix A)

The CONTAM Panel has further discussed possible bias in case-control studies in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' (EFSA CONTAM Panel, 2015).

> *Lines 6147-8 refer to assessment of habitual diet 20 years before interview by a validated food frequency questionnaire. A comment about the reliability of such data should be incorporated* (see comment 86 in Appendix A)

The CONTAM Panel has now specified that dietary information in the distant past (chosen by the authors to reflect latency between exposure and cancer) has been shown to have a fairly good reliability, although lower than the reliability of current dietary information, and referred to the study by Wolk et al. (1997) in Section 7.4.1.2 on 'Dietary studies and cancer' (EFSA CONTAM Panel, 2015). The issue of recall bias in case-control studies is discussed in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' (EFSA CONTAM Panel, 2015).

> *The major limitation of the evidence above anything else is exposure misclassification and this should be mentioned at the start of the limitations due to limitations in estimation of both dietary and non-dietary exposure sources. Exposure misclassification is likely to have resulted in bias towards the null and it would be helpful to discuss if this is the key factor in why epidemiological studies in the general population have not found cancer risks (in contrast to animal studies), or whether this is a question of dose* (see comment 86 in Appendix A)

The CONTAM Panel agrees that exposure misclassification is an important issue in the discussion of the epidemiological studies. Section 7.4.1.2.7 of the opinion (EFSA CONTAM Panel, 2015) now discusses the possible sources of exposure misclassification. The Panel agrees that exposure misclassification most likely would have caused a bias towards the null (i.e. lead to an underestimation of the strength of an association). The CONTAM Panel however considers that it is not possible to discern whether study power, exposure misclassification and/or the magnitude of exposure could explain the observation that some epidemiological studies have not found increased cancer risks in humans as predicted from the animal cancer bioassays, while others have.

3.6.3. Comments related to the dietary studies and pre-natal exposure

> *When reviewing reproductive and developmental outcomes, background data on associations of relevant outcomes with smoking might provide an upper estimate of risk for effects from dietary exposures to acrylamide* (see comment 83 in Appendix A)

The Panel noted that Pedersen et al. (2012) reported a reduction in birth weight in newborn children for the highest quartile versus the lowest quartile of AA adducts which was comparable with the reduction in birth weight observed for children exposed in utero to maternal smoking, and this has been indicated in Section 7.4.2.1 on 'Developmental consequences' (EFSA CONTAM Panel, 2015). However, the CONTAM Panel does not find it appropriate to use the association of relevant outcomes with smoking as background data. Smoke contains thousands of bioactive substances with heterogeneous and combined effects on reproductive and developmental outcomes. There would be too many uncertainties in using these data as a reliable upper estimate.

It should be considered whether caffeine could have been the cause of the effects observed in the Norwegian Mother and Child Cohort (see comment 88 in Appendix A)

The CONTAM Panel notes that in the Norwegian Mother and Child Cohort (NMCC) intake of coffee was measured, but not the type of coffee (i.e. caffeine content). Caffeine intake is associated with a modest although significant increase of unfavourable birth outcomes, although it is still unclear whether this association is causal (Greenwood et al., 2014). The published analyses from the NMCC were adjusted for coffee intake, but residual confounding related to caffeine content cannot be excluded. The CONTAM Panel has therefore added a remark in this respect in Section 7.4.2.1 (EFSA CONTAM Panel, 2015).

It is suggested to complete the description of the study by Pedersen et al. (2012) in Section 7.4.2.1 on 'Epidemiological studies: developmental consequences' to indicate that (i) 'both AA and GA adducts were significantly association with increased risk of being small for gestational age', and that (ii) 'monotonic dose–response associations of AA exposure with birth outcomes were observed in women who were nonsmokers in pregnancy, as well as in never-smokers, even after adjusting for passive smoking based on self-reporting or using ethylene oxide Hb adducts as biomarkers of exposure to tobacco smoke. The associations between AA exposure and birth weight were consistent across the five countries." (see comment 89 in Appendix A)

The CONTAM Panel has introduced this additional information into the opinion (EFSA CONTAM Panel, 2015) for the sake of completeness.

We would like to inform you that a study, which is not yet published, but it is in preparation, with the French EDEN mother-child cohort have estimated maternal intake of AA using FFQ and that the authors have informed us that their findings are in line with those cited by Pedersen et al. 2012 and Duarte-Salles et al 2013. In this French study of 1,471 mother-child pairs, maternal intake of AA has been assessed by combining FFQ data on maternal dietary habits with data on AA concentration in foods provided by the second French total diet study (see comment 89 in Appendix A)

The CONTAM Panel notes that the study mentioned in this comment had not been published in a peer-reviewed journal by the cut-off date of inclusion of published evidence (13 March 2015, EFSA CONTAM Panel, 2015). It has therefore not been possible to include the findings of this study in the opinion.

3.6.4. Comments related to the dietary studies and neurological alterations

Data on exposures resulting in neurotoxicity, or discussion of why such exposures cannot be meaningfully characterised, would be helpful (see comment 90 in Appendix A)

Is the proposed critical BMDL for neurological effects in rats likely to be lower than the exposures that have given rise to human neurotoxicity (see comment 92 in Appendix A)

The CONTAM Panel notes that the human studies which indicated exposures that have given rise to neurotoxicity, such as Calleman et al. (1994) and Hagmar et al. (2001), have methodological deficiencies and uncertainties, and therefore the data are not reliable for the purpose of establishing a

reference point for AA-induced neurotoxicity. For example, the subjects were reported to have been exposed to other compounds such as acrylonitrile, and were exposed by different routes (e.g. dermal and inhalation exposure). It is also noted that these studies are difficult to compare to the better controlled exposures of most animal studies.

3.7. Comments related to the benchmark dose modelling (BMD)

> *It is not clear why, with several recent reproductive studies investigating the same dose range and showing effects, no attempt to calculate a BMD10 for male fertility effects is made. In section 7.5.2. Dose-response assessment it is stated that "The data on effects of AA on male reproduction were not suitable for dose-response modelling" however, no clear explanation is provided about why deriving a BMD10 is unfeasible* (see comment 75 in Appendix A)

The CONTAM Panel notes that the data on reproductive toxicity are not suitable for dose-response modelling since e.g. in the two generation reproductive toxicity study, effects were seen at the highest dose only. In some other studies there was no dose-response, only two doses were tested, and few animals were used in the experiments. The CONTAM Panel concluded also that there was too much uncertainty about the biological relevance of the findings in the 90-day AA dietary intake study (NTP, 2012) to be used to establish a reference point for use in the risk characterisation. No dose-response modelling was performed on the data on developmental toxicity due to the limitations identified in the studies (e.g. no dose-response was observed, only two doses were tested, or effects were observed only at the highest dose). To increase clarity, the text in Sections 7.3.5 on 'Reproductive and developmental toxicity' and 7.5.2 on 'Dose-response assessment' has been revised (EFSA CONTAM Panel, 2015).

> *It is not clear from Appendix K why the Harderian gland had been selected, as lower BMDL values were obtained for mammary gland fibroadenomas in rats, which appeared to be equally appropriate to use. It is recommended that more clarification should be given about the choice of BMDL* (see comment 70 in Appendix A)

To increase clarity, the text in Appendix K of the opinion has been revised to provide a better rationale for the selection of the $BMDL_{10}$ value used in the opinion as a reference point (EFSA CONTAM Panel, 2015).

3.8. Comments related to the risk characterisation

Several entries related to the section on the risk characterisation.

> *As the concept of MOE is not well understood by people who are not toxicologist, it would assist the risk managers to use a more descriptive language to communicate the EFSA Panels level of concern in their final risk characterization* (see comment 91 in Appendix A)

The CONTAM Panel notes that the approach taken is consistent with the Panel's usual approach in accordance with the Opinion of the EFSA Scientific Committee related to a harmonized approach for risk assessment of substances which are both genotoxic and carcinogenic (EFSA, 2005).

> *In the abstract it would be helpful to add to the end of the last sentence adding 'based on evidence from animal studies'. As currently written, and for the reader unfamiliar with toxicological evidence who may only read the abstract, the current wording could be confusing as it discusses no evidence of carcinogenicity from human studies but then raises concern about neoplastic effects* (see comment 1 in Appendix A)

The CONTAM Panel finds this addition to the abstract appropriate to increase clarity (EFSA CONTAM Panel, 2015).

Given the uncertainties in the acrylamide dietary exposure and the evolving state of understanding of acrylamide toxicity, EFSA is encouraged to ensure that the final scientific opinion make it clear that there is no conclusive evidence that acrylamide presents any human safety concern at the current levels of dietary exposure (see comment 67 in Appendix A)

The CONTAM Panel considered the uncertainties and limitations in the data used to perform the risk assessment of AA in food. These are described and discussed in the opinion. Taking all this into consideration, although the human studies have not demonstrated AA to be a human carcinogen, the MOEs across dietary surveys and age groups indicate a concern with respect to neoplastic effects based on mechanistic information and evidence from animal studies.

The recommended values of 0.43 ppm for Neurotoxic effects is equal to 430 ppb per kg, i.e. for an adult who weighs 70 kg, daily intake should be up to 30,100 ppb. In addition, recommended value of 0.17 ppm for Neoplastic effects equals to 170 ppb for an adult who weighs 70 kg and intake should be up to 11,900 ppb. The recommended values from 2013/647/EU commission are hence adequate since enable a daily intake of products under the risk limits (0.17 mg/kg) (see comment 95 as in Appendix A)

The CONTAM Panel wishes to clarify that the values of 0.43 and 0.17 mg/kg b.w. per day are not 'recommended values', but are the reference points used to calculate the MOEs. In contrast, the values laid down in Commission Recommendation 2013/647/EU are 'indicative values' which are not safety thresholds, but only intended to indicate the need for an investigation of the AA source.

3.9. Comments related to the uncertainty section

Several comments were made in relation to the section on uncertainty in the risk assessment as follows.

In Section 9.4 on 'Other uncertainties', suggesting that studies in which estimated dietary acrylamide intake (e.g. assessed with an FFQ) is correlated to AA Hb adducts are "validation studies" is overreaching (see comment 96 in Appendix A)

The CONTAM Panel considers that the studies comparing FFQ estimates of AA with Hb adducts cannot be considered validation studies and thus deleted the sentence "as shown in the few validation studies performed". Moreover, in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' (EFSA CONTAM Panel, 2015), the Panel has further addressed the limitations of correlations between FFQs and Hb adduct measurements and quoted the study by Vikström et al. (2012) (which was already described in detail in Section 7.2.2.2).

In Section 9.4 on 'Other uncertainties', uncertainties in the measurement of AA intake in epidemiological studies may hamper reliably assessing its relation with cancer risk, but it is important to stress that this will only lead to underestimation of the strength of an association when one is found (see comment 96 in Appendix A)

The CONTAM Panel has modified the sentence in Section 7.4.1.2.7 on 'Considerations on the interpretation of the epidemiological studies' to indicate more clearly that such misclassifications tend to lead to an underestimation of the strength of an association (EFSA CONTAM Panel, 2015).

In Section 9.4 on 'Other uncertainties', it is questionable to state that the fact that the occupational epidemiological studies did not observe clear risks contributes to the uncertainty whether acrylamide is a human carcinogen. These occupational studies namely included nearly only men and were thus not able to show risks in women (e.g., endometrial cancer), if any. Studies in rats/mice are also performed in both sexes for a reason, I would say (see comment 96 in Appendix A)

The CONTAM Panel has addressed this comment in Section 9.4 on 'Other uncertainties' indicating that the occupational studies generally included only men, and were thus not able to analyse possible risk of endometrial and ovarian cancer.

> *Considering the fact that multiple dietary epidemiological studies of good quality showed associations with cancer risk (mainly endometrial, ovarian cancer) and that the 2 studies on developmental toxicity (birth outcomes) performed so far showed clear reductions in prenatal growth, the impact of the uncertainties on the risk assessment of human exposure to AA through consumption of food is not moderate, but major. The risks of cancer in the epidemiological studies are namely much higher than calculated based on the rodent data (based on the rodent calculations, risks would be so low that they could never have been picked up in epidemiological studies, yet they were in some studies). In addition, if the epidemiological associations between dietary acrylamide intake and birth outcomes are true, then there is no MOE for developmental exposure at all. Can EFSA with absolute certainty exclude the possibility that humans are more sensitive to acrylamide than rodents?*
>
> *The mentioned uncertainties are miniscule compared to the uncertainty that is introduced by disregarding the epidemiological findings in the way that is done in this opinion. The studies on cancer may be limited and inconsistent and it may not be clear if the association between dietary AA exposure and birth outcomes is causal, but that does not mean that the findings can be ignored in the risk assessment and certainly not in the assessment of the uncertainties associated with the risk assessment done* (see comment 96 in Appendix A)

The epidemiological evidence has not been disregarded in the opinion. The epidemiological studies available for the risk assessment were described and their limitations discussed. The CONTAM Panel concluded that they were not adequate as the basis to establish a reference point, and the animal data were therefore used. Since the animal data indicate a concern, the uncertainty from the human data does not have a major impact on the overall risk assessment.

The approach taken by the Panel for the risk characterisation, e.g. by using the MOE, assumes that humans could be more sensitive than experimental animals.

> *It would be useful to summarise the most important sources of uncertainty* (see comment 97 in Appendix A)

The CONTAM Panel has summarised the main sources of uncertainty in the risk assessment of AA in food in Section 9 of the opinion in a qualitative way indicating the direction of the uncertainty, i.e. whether it has potential to cause over- or under-estimation of exposure/risk.

> *It is unclear why the entry relating to occupational studies in Table 31 indicates underestimation of exposure* (see comment 98 in Appendix A)

The CONTAM Panel considers that the lack of support from the occupational studies for the major critical effects, except for neurotoxicity, is an uncertainty with potential to cause both over- and under-estimation of the risk, and has therefore amended Table 31 in Section 9.5 on 'Summary of uncertainties' (EFSA CONTAM Panel, 2015).

3.10. Comments related to the conclusions and recommendations

Several comments related to the conclusions and recommendations made by the CONTAM Panel in the draft opinion, or on further recommendations considered to be relevant for inclusion in the risk assessment as follows.

> *In the recommendations the CONTAM Panel asks for better reporting data for a more accurate exposure assessment, which is certainly justified for pure science, but is not of high priority for the consumers* (see comment 9 in Appendix A)

The CONTAM Panel noted a number of uncertainties in the reported occurrence data regarding the preparation of the respective food commodities which has an impact on the estimated exposure. This was specially the case for French fries. A more accurate exposure assessment would be helpful to study a time trend in the exposure, and eventually to assess whether mitigation measures are effective.

> *Is EFSA not of the opinion that more epidemiological studies on dietary acrylamide intake and cancer risk are needed?* (see comment 99 in Appendix A)

Given the available evidence regarding dietary exposure to AA and the risk of certain types of cancer (e.g. endometrial, ovarian and renal cell), the CONTAM Panel considers it appropriate to recommend further epidemiological studies (EFSA CONTAM Panel, 2015). Such studies should have an improved measurement of AA exposure, and should be sufficiently powered.

> *What is the opinion of EFSA on epidemiological studies on dietary acrylamide intake and neurotoxicity? Richard LoPachin has repeatedly suggested in his papers that studies in this field are indicated. Considering the fact that studies in workers have shown effects on the central nervous system and the fact that these effects may not be reversible and are thus cumulative over time suggests that chronic high dietary acrylamide intake may be able to contribute to neurological diseases such as Alzheimer's and Parkinson's disease. In addition, acrylamide could perhaps also lead to impaired cognitive development* (see comment 99 in Appendix A)

Because of general pathophysiological considerations, LoPachin and DeCaprio (2005) hypothesized that AA exposure may be related to the development of Alzheimer's or Parkinson's disease or related neurological disorders. The CONTAM Panel did not identify any evidence to support this hypothesis.

> *Further recommendations could include: (i) adequate data on the AA effects on reproductive development and maturation (from organogenesis to puberty), (ii) clarification on the relevance of possible endocrine-related mechanisms for reproductive and developmental effects as well as for tumour development in specific target tissues in rodents and humans, (iii) clarification on developmental neurotoxicity mechanisms and on the link between early molecular/structural changes and possible adverse outcomes in later life* (see comment 100 in Appendix A)

The CONTAM Panel considers it appropriate to include a recommendation in the opinion for an up-to-date extended one-generation or two-generation reproductive toxicity study to investigate the effects of AA on sperm parameters, including a detailed histopathological examination of the testis and accessory glands, as well as investigating the effects on development until puberty (EFSA CONTAM Panel, 2015). The CONTAM Panel has highlighted in the 'Recommendations' the aspects that it considered to be key priorities for the risk assessment of dietary exposure to AA. Clarification on the relevance of possible endocrine-related mechanisms for reproductive and developmental effects as well as for tumour development in specific target issues in rodents and humans is not considered a priority in this context as it will not change the approach to the risk assessment.

> *Given the effects on the rodent testis, a comment on the possibility of transgenerational effects, would be useful together with a recommendation for research* (see comment 106 in Appendix A)

The CONTAM Panel noted this remark was already discussed in the draft opinion. The Panel recognised the possibility of transgenerational effects of AA noting that AA is a germ cell mutagen. The CONTAM Panel noted that at present there are no established procedures for risk assessment using this endpoint, and recommended the development of improved approaches for the detection and risk assessment of germ cell mutagens, and these be applied to AA and GA.

> *How useful is a risk assessment without any recommendations? The risk manager is usually not an expert in epidemiology, exposure assessment and toxicology. Did DG Sanco ask for a new risk assessment without wishing a recommendation from the scientists, judging their findings and contemplating the options to reduce the risk? What does it mean if acrylamide is called a*

"concern", but no consequences follow? Does EFSA really not recommend any risk management action facing a MOE which is below 500? The BfR developed guidelines for risk assessments which provide a recommendation in every case. Consequently, it has to be mentioned explicitly when no action is recommended (BfR, 2010). Why was the concept of MOE introduced if even at a low MOE no recommendation is given? How low must the MOE be before any recommendation will be given? (see comments 16, 51, 52, 84, 107 and 108 in Appendix A)

The CONTAM Panel made a number of recommendations in view of data and knowledge gaps, to improve the risk assessment of AA in food. The term 'recommendation' mentioned in this comment refers more to mitigation measures. The CONTAM Panel notes that the evaluation of such measures and estimation of their effects on the exposure of the population was not included in the terms of references for this Scientific Opinion, and were therefore not addressed in the risk assessment. The evaluation of mitigation measures and their effects are, in this specific case, under the remit of the European Commission.

Regarding the question *How much progress was made compared to the 1994 risk assessment by IARC?* made in comment 16, the CONTAM Panel wants to clarify that IARC (1994) did not perform a risk assessment on AA in food, but evaluated only its carcinogenicity on the data available at that time.

CONCLUSIONS

Following the comments received during the public consultation, a revised version of the opinion on AA in food was produced and adopted by the CONTAM Panel on 30 April 2015, during its 71st CONTAM Panel meeting.

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APPENDICES

Appendix A. Table of comments

Table of comments received during the public consultation on the draft Scientific Opinion on acrylamide in food. Comments are organised by sections of the opinion.

N	Contributor	Section	Comment received
1	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Abstract	This response combines the views of the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) and Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment (COC). Both COT and COC commented on the high quality and comprehensive nature of the scientific opinion and were broadly in agreement with the evaluation and conclusions reached. They made recommendations for improvements in a number of areas, particularly relating to other potentially significant exposure sources. As a minor point, the use of AA as an abbreviation for acrylamide seems unnecessary and makes the document harder to read. Abstract: It would be helpful to add to the end of the last sentence ending '*...with respect to neoplastic effects*', the phrase '*based on evidence from animal studies*.' As currently written, and for the reader unfamiliar with toxicological evidence who may only read the abstract, the current wording could be confusing as it discusses no evidence of carcinogenicity from human studies but then raises concern about neoplastic effects.
2	FoodDrinkEurope (FDE)	Abstract	Lines -5-23: Both in the abstract and the summary (lines 28-241) product categories with the 'highest levels' are highlighted; however these are not always the products which contribute the largest amounts to dietary intakes. FoodDrinkEurope finds it important that the context of this draft Scientific Opinion, to provide at least equal emphasis within the abstract and summary to those product categories which have been calculated to contribute significant amounts to dietary intake. We also believe that the recommendations presented on Page 192 (Lines 7369 to 7380) are very important and should receive greater emphasis within the abstract and within the summary. Lines 9-10: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only.

			The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): • Roasted coffee (dry): 249 • Instant coffee (dry): 710 • Substitute coffee (dry), based on cereals: 510 • Substitute coffee (dry) based on chicory: 2942 • Substitute coffee (dry) unspecified: 415 It has to be noted that the markets for coffee and for coffee substitutes are hugely different in volume. Based on Eurostat/Prodcom data we calculate that the size of the coffee substitutes market is 2,3% of that of the coffee market. The statement that AA was found at the highest levels in 'Coffee and coffee substitutes' gives the impression that this is the case across all sub-categories, while in fact it is correct only for the much smaller market of the chicory-based coffee substitutes. We therefore propose: • To split the 'coffee and coffee substitutes' into the two sub-categories. • To refer to acrylamide levels in coffee and in coffee substitutes as consumed The statement that AA was found at the highest level in 'coffee and coffee substitutes' should be revised accordingly. Lines 8 – 9: FoodDrinkEurope supports the further collection of accurate data on consumption in relation to diet contribution and would welcome a clearer indication which reflects this distinct contribution of different food

			categories.
3	National Coffee Federation USA (NCA)	Abstract	2. Abstract, line 9-10: The food category "coffee and coffee substitutes" is comprised of several subcategories with very different AA levels in the dry product. As shown in Table 6 (line 1359), the mean value for "roasted coffee (dry)" is 249 micrograms per kilogram (µg/kg), as compared to mean values of 710 µg/kg for "instant coffee (dry)," 510 µg/kg for "substitute coffee (dry), based on cereals," 2,942 µg/kg for "substitute coffee (dry), based on chicory," and 415 µg/kg for "substitute coffee (dry), unspecified." These data clearly indicate that AA levels differ between these categories, particularly substitute coffee based on chicory. We recommend that "coffee" and "substitute coffee" be treated as separate food categories.
4	Austrian Agency for Health and Food Safety (AGES)	Abstract	Lines 14/15: To what extent is AA metabolised by conjugation with glutathione and to what extent by epoxidation to glycidamide? Do you have information about this? If yes, could this information be implemented into the opinion?
5	European Coffee Federation (ECF)	Abstract	Line 9-10: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only. The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): - Roasted coffee (dry): 249 - Instant coffee (dry): 710

			- Substitute coffee (dry), based on cereals: 510 - Substitute coffee (dry) based on chicory: 2942 - Substitute coffee (dry) unspecified: 415 It has to be noted that the markets for coffee and for coffee substitutes are hugely different in volume. Based on Eurostat/Prodcom data we calculate that the size of the coffee substitutes market is 2,3% of that of the coffee market. The statement that AA was found at the highest levels in 'Coffee and coffee substitutes' gives the impression that this is the case across all sub-categories, while in fact it is correct only for the much smaller market of the chicory-based coffee substitutes. We therefore propose: - To split the 'coffee and coffee substitutes' into the two sub-categories. - To refer to acrylamide levels in coffee and in coffee substitutes as consumed The statement that AA was found at the highest level in 'coffee and coffee substitutes' should be revised accordingly.
6	LTD H-Group	Abstract	Implement state monitoring and supervision over the quality and innocence of the drinking water. - Give to the water qualification of product category. (I am the member of the experts council giving the water product category, according the 23/05.2007 order #2-70 of minister of agriculture). - Provide supervision, control and monitoring over producing food, alcohol, nonalcoholic, semi processed goods and carbon dioxide. - Work out the plan for ruling the critical situation, including establishing the crisis ruling group. - Take preventive and coordinating measures considering general principles of food innocence in order avoid risks. - Systematically inform population about high risk or harmful food. - Informing population about current issues of food innocence. - Informing producers/distributers and customers about legal demands in the field of innocence food. - Bring to light the facts of falsifications and taking measures.
7	Kantolanes Labor Zurich	Abstract	Line 7, but also repeated later (lines 34, 432, 864, 1645): In the literature it is often mentioned that AA-formation starts being relevant at temperatures above 120 °C. No reference is cited to support this. It could be that this was from our early work [1]. It is, however, not really correct. As mentioned above, with ammonium carbonate in a dry matrix AA formation occurs at clearly lower temperature. More important (and hardly ever mentioned) is the absence of water, e.g. crust formation: water impedes AA-

			formation. In [1] we have shown that cooking wet potato at 120 °C (under pressure) formed <20 µg/kg AA, while it formed about 10,000 µg/kg when heating dry potato powder. Hence often a minimum of 120 °C is needed to efficiently evaporate water and form a crust – not the temperature as such is relevant, but evaporation of water. This explains why AA formation in chips, French fries and bakery ware is mainly formed in the last moment when a dry crust has been formed (shown, e.g., in [2]). [1] Methods for determining the potential of acrylamide formation and its elimination in raw materials for food preparation, such as potatoes. M. Biedermann, S. Biedermann-Brem, A. Noti, and K. Grob. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 93 (2002) 653-667. [2] Influence of the frying temperature on acrylamide formation in French fries. K. Fiselier, D. Bazzocco, F. Gama-Baumgartner, K. Grob. Eur. Food Res. Technol. 222 (2006) 414-419.
8	European Coffee Federation (ECF)	Summary	Line 46-47: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only. The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): - Roasted coffee (dry): 249 - Instant coffee (dry): 710 - Substitute coffee (dry), based on cereals: 510 - Substitute coffee (dry) based on chicory: 2942

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9	Kantonales Labor Zurich	Summary	Lines 233 and 7369: recommendations. An enormous amount of money has been invested into research dealing with AA, but so far the consumers have profited little. It has repeatedly been stated that AA is one of the most toxic substances in food, but risk managers do not react accordingly. There are an industry toolbox and numerous papers showing options for mitigation, but in the EU the proposals are hardly implemented. EFSA is aware of this, but in this draft opinion it missed the opportunity to address the problems behind taking measures. In the recommendations the CONTAM Panel asks for better reporting data for a more accurate exposure assessment, which is certainly justified for pure science, but is not of high priority for the consumers. For these it is a bit like the fire brigade being in front of a burning building with an armada of all sorts of vehicles and all they do is mapping temperature in the various parts of the flames; and as the destruction proceeds, the commander asks for a better method of measurement. In the present situation (after 12 years of broad research), the most useful work of EFSA would be the evaluation of options for mitigation and estimation of their effect on exposure for the concerned groups of consumers. The opportunity to do this with the present opinion is probably gone, but it could be the main recommendation for further work. It is not easy to devise measures for implementing mitigation. Just for illustration: the specification of legal limits for AA might be reasonable for coffee and potato chips (whereby at least for chips it would probably have to be on an average rather than to cut off single extremes, which is more complicated to implement). However, in both cases the

			potential for improvement seems limited. Legal limits for AA are probably not meaningful in most other areas. Firstly, these limits would have to be far above the level that can be considered safe by EFSA standards. Such limits not only restrict against high concentrations, but also authorize up to this level. Secondly, a legal limit for, e.g., French fries or bakery ware would presuppose that many 100,000 producers (the person at the fryer or small bakeries) would have to repeatedly check compliance. Thirdly, AA formation in the domestic kitchen cannot be regulated. Hence finding appropriate measures and estimating their potential of improvement is a key subject and should be tackled by EFSA, advising the risk managers. Measures probably have to be system-related. For instance, ammonium strongly increases AA formation and it could be required that in bakery ware prepared with ammonium carbonate asparaginase is used (as already done for a few products). For fried or roasted potato products, low contents in reducing sugars are a key requirement which can be implemented by selection of suitable varieties and primarily by storage conditions optimized for the application (avoidance of low temperatures); legal limits for reducing sugars would probably be more effective than for AA. Fryers can be constructed to have a better temperature profile (falling rather than increasing temperature towards the end of frying, as used by chip producers, since most of the AA is formed during the last seconds of the process [ ]). There are probably many more ways to be taken into consideration.
10	Istituto Superiore di Sanità (ISS)	Summary	Lines 184-193: The opinion is overall sound and thoughtful, and it surely represents a step forward with regard to the protection of consumers from exposure to process contaminants. However, improvements are suggested concerning the assessment of reproductive and developmental effects, since these might be relevant to the risk characterization for specific, potentially vulnerable lifestages (pregnancy, peripubertal). Specific comments are made in the relevant sections.
11	FoodDrinkEurope (FDE)	Summary	Lines -5-23: Both in the abstract and the summary (lines 28-241) product categories with the ‘highest levels’ are highlighted; however these are not always the products which contribute the largest amounts to dietary intakes. FoodDrinkEurope finds it important that the context of this draft Scientific Opinion, to provide at least equal emphasis within the abstract and summary to those product categories which have been calculated to contribute significant amounts to dietary intake. We also believe that the recommendations presented on Page 192 (Lines 7369 to 7380) are very important and should receive greater emphasis within the abstract and within the summary.

			Lines 9-10: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only. The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): • Roasted coffee (dry): 249 • Instant coffee (dry): 710 • Substitute coffee (dry), based on cereals: 510 • Substitute coffee (dry) based on chicory: 2942 • Substitute coffee (dry) unspecified: 415 It has to be noted that the markets for coffee and for coffee substitutes are hugely different in volume. Based on Eurostat/Prodcom data we calculate that the size of the coffee substitutes market is 2,3% of that of the coffee market. The statement that AA was found at the highest levels in 'Coffee and coffee substitutes' gives the impression that this is the case across all sub-categories, while in fact it is correct only for the much smaller market of the chicory-based coffee substitutes. We therefore propose: • To split the 'coffee and coffee substitutes' into the two sub-categories. • To refer to acrylamide levels in coffee and in coffee substitutes as consumed FoodDrinkEurope supports the further collection of accurate data on consumption in relation to diet contribution and

			would welcome a clearer indication which reflects this distinct contribution of different food categories.
12	National Coffee Association USA (NCA)	Summary	1. Summary, line 46-47: The statement that, "AA was found at the highest levels in 'Coffee and coffee substitutes', followed by 'Potato crisps and snacks' and 'Potato fried products'" may be technically correct. However, it is very misleading because the levels in coffee and coffee substitutes are based on the dry product whereas the levels for potato crisps and snacks and potato fried products are based on the products as prepared for consumption. An "apples-to-apples" comparison of AA levels in coffee and coffee substitutes as consumed to AA levels in other consumed foods would show that many other food categories contain higher AA levels relative to coffee and coffee substitutes. We recommend that all comparisons of AA levels in different food categories be made in terms of food or beverage "as consumed" and that the statement "AA was found at the highest levels in 'Coffee and coffee substitutes'," be revised accordingly.
13	National Coffee Association USA (NCA)	Summary	2. Summary, line 46-47: The food category "coffee and coffee substitutes" is comprised of several subcategories with very different AA levels in the dry product. As shown in Table 6 (line 1359), the mean value for "roasted coffee (dry)" is 249 micrograms per kilogram (µg/kg), as compared to mean values of 710 µg/kg for "instant coffee (dry)," 510 µg/kg for "substitute coffee (dry), based on cereals," 2,942 µg/kg for "substitute coffee (dry), based on chicory," and 415 µg/kg for "substitute coffee (dry), unspecified." These data clearly indicate that AA levels differ between these categories, particularly substitute coffee based on chicory. We recommend that "coffee" and "substitute coffee" be treated as separate food categories.
14	Novozymes A/S	Introduction	Novozymes is grateful to EFSA for the opportunity to provide feedback to the present public consultation on acrylamide. As a leading enzyme producer, Novozymes has developed enzymatic solutions to reduce acrylamide occurrence in foods. The use of asparaginase in the manufacturing of several types of foods and food ingredients is indeed mentioned in the FoodDrinkEurope toolbox. We will only provide input on section 4 of the EFSA draft scientific opinion – to give concrete examples of the usefulness of the asparaginase technology and shed some light on incoming improved enzyme solutions.
15	FoodDrinkEurope (FDE)	Introduction	Lines 402 -404: FoodDrinkEurope finds it important to mention also that these brochures are available in 23 European languages and that industry has contributed to important DG research or national research programmes, such as Heatox (http://heatox.org/), and Prometheus (http://www.eusem.com/body/CS/EUproj/PROMETHEUS.htm) as well as a project to control asparagine in wheat. Other efforts concern cooking instructions to help consumers reducing their exposure to acrylamide (www.goodfries.eu); which is available in 28 languages.

16	Anonymous	Introduction	In 2002, acrylamide was known as a substance which damages nerves (Friedman, M., 2003; LoPachin, 2004) and which is able to change the genetic material of cells irreversibly (BgVV, 2002 a). It was classified as „probably carcinogenic“ to humans by IARC (1994). This assessment was non-controversial among experts (Rudén, 2004), and after the discovery of acrylamide in food WHO (2002) consequently recommended to reduce the exposition. At the same time, many research questions were raised (e.g. BgVV 2002 a; WHO, 2002; SCF, 2002; VWA, 2003). Several questions addressed urgent issues: How does acrylamide gets into the food? How can we measure it? Which kinds of food are affected? How can we reduce it? The answers to many other research questions would have been helpful to better determine the risk related to acrylamide, but one could predict that answers could not be found within a certain timeframe: What is the mode of action as a carcinogen? Is the extrapolation of data gathered from animals to the human situation appropriate? Exactly how much acrylamide do we ingest? Is acrylamide carcinogenic to humans? The second type of research questions poses crucial questions: Did the consumer benefit from twelve years of research? How much progress was made compared to the 1994 risk assessment by IARC? EFSA’s latest risk assessment offers the opportunity to address these questions. (This is actually not a comment on the chapter "Introduction" but an introduction to my comment. Please read my comment as a whole. I sent it via E-Mail) References: – BgVV - Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin, 2002: Zum Vorkommen von Acrylamid in Lebensmitteln. Bericht des Bundesinstituts für gesundheitlichen Verbraucherschutz und Veterinärmedizin über das Expertenge-spräch vom 14. Mai 2002 [About Acrylamide in Food. Report about the experts’ meet-ing on Mai, 14th, 2002]. In: http://www.bfr.bund.de/cd/3862?index=65&index_id=4185, accessed September 2014 – Friedman, Mendel, 2003: Chemistry, Biochemistry, and Safety of Acrylamide. A Re-view. In: Journal of Agricultural and Food Chemistry, Vol. 51, Issue 16, 4504-4526 – IARC - International Agency for Research on Cancer, 1994: Acrylamide. IARC Mono-graphs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, 60. Lyon, France: IARC. In: http://monographs.iarc.fr/ENG/Monographs/vol60/index.php, ac-cessed September 2014 – LoPachin, Richard M., 2005: Acrylamide Neurotoxicity: Neurological, Morhological and Molecular Endpoints in Animal Models. In: Friedman, M. & Mottram, D. (Hrsg.): Chemistry and Safety of Acrylamide in Food.

			Advances in Experimental Medicine and Biology, Vol. 561. Heidelberg, New York: Springer, 21-38 – Rudén, Christina, 2004: Acrylamide and cancer risk — expert risk assessments and the public debate. In: Food and Chemical Toxicology, Vol. 42, Issue 3, 335-349 – SCF - Scientific Committee on Food, 2002: Opinion of the Scientific Committee on Food on new findings regarding the presence of acrylamide in food, expressed on 3 Juli 2002. In: http://europa.eu.int/comm/food/fs/sc/scf/out131_en.pdf, accessed September 2014 – VWA - Food and Consumer Product Safety Authority, 2003: White paper on acrylami-de - Presented to the EFSA Advisory Forum for consideration. Outcome of the acryl-ami¬de workshop held in Brussels on March 28, 2003. In: http://www.efsa.europa.eu/en/af030703/docs/af030703-ax8.pdf, accessed September 2014 – WHO - Word Health Organization in collaboration with the Food and Agriculture Or-ganization of the United Nations: Health implications of acrylamide in food. Joint FAO/WHO consultation, Geneva, Switzerland, 25 - 27 June 2002. In: http://www.who.int/topics/acrylamide/en/, accessed September 2014
17	FoodDrinkEurope (FDE)	Previous risk assessments	Line 746: Reference has been made to the Danish DTU publication - indicating that is was found that 'For adults, the food category contributing most to the intake was potato products, followed by coffee and cocoa. …'. This may suggest that cocoa has been identified in Denmark to be a major contributor. But when reading the original Danish report, it says in more detail the contribution from potato products is 'followed by coffee and cocoa at 30 % of which coffee contributes the most.'' Our suggestion: "For adults, the food category contributing most to the intake was potato products, followed by coffee and cocoa, of which according to the DTU publication coffee contributes the most".
18	Kantonales Labor Zürich	Formation in Food	In [1] we investigated the formation and elimination of AA in model matrices, such as potato powder, wheat flour and corn starch, with the addition of fructose, glucose, sucrose, asparagine and numerous other components. The influence of temperature on formation as well as elimination of AA was also studied. The main outcome of practical relevance was that ammonium carbonate or ammonium bicarbonate used to raise dough increases the yield of the reaction to AA in bakery ware roughly 10 times. AA formation was substantial at temperatures as low as 80 °C. It was confirmed that the bakery ware and cereals with high AA contents are mostly made with these salts [2]. Ammonium might also contribute to the high AA-formation in potato products. For many products it seems possible to avoid the use of ammonium carbonate, but for others, like gingerbread, it is

			essential for the product identity. In these cases the removal of asparagine by asparaginase seems suitable. [1] Model studies on acrylamide formation in potato, wheat flour and corn starch. M. Biedermann and K. Grob. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 94 (2003) 406-422. [2] Acrylamide monitoring 2007-2009 in Switzerland: results and conclusions. M. Biedermann, F. Grundböck, K. Fiselier, S. Biedermann, Ch. Bürgi, and K. Grob. Food Additives Contaminants 27 (2010) 1352-1362
19	Kantonales Labor Zürich	Formation in Food	In line 878 it is mentioned that the ratio of fructose to glucose impacted both color and AA levels. In fact fructose more efficiently supports AA formation than glucose, but glucose also efficiently supports elimination. Elimination is neglected in the draft opinion: as we have shown in [1,2], easily 50-80 % of the AA is eliminated concurrently with formation (in meat products probably close to 100 %). Thus elimination may be as determinant for the final AA concentration as formation (which is usually recognized for coffee). [1] Methods for determining the potential of acrylamide formation and its elimination in raw materials for food preparation, such as potatoes. M. Biedermann, S. Biedermann-Brem, A. Noti, and K. Grob. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 93 (2002) 653-667 [2] Model studies on acrylamide formation in potato, wheat flour and corn starch. M. Biedermann and K. Grob. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 94 (2003) 406-422
20	Kantonales Labor Zürich	Legislation	In line 961 it is stated that AA used in food contact materials is restricted by the generic specific migration limit of 60 mg/kg of food. This is wrong: AA must not be detectable in food, whereby the detection limit is 0.01 mg/kg.
21	Chilean Food Quality and Safety Agency (ACHIPIA)	Sample collection and frequency	Sampling must be highly standardised so studies can be comparative to each other, in order to provide comparable results of Acrilamide (AA) content per food as accurate as possible. In this regard, it is proposed to establish statistic sampling designs, detailing sampling type, time, product condition and kind of product in order to reduce uncertainty on the results. For example, flakes made in laboratory show up to 1200 ppb of AA vs 500 ppb in commercial products. Great part of the work reported in different publications could thus inform greater concentrations of AA than the real amount in a commercial product, over alarming the population. Since the European Commission recommends sampling products at market level, it would be interesting to correlate the contents of AA found in commercial products with the process conditions used for its production, as well as it is

			important to carry out the procedure according to the sampling aproved by trademarks in different batches over a period, considering that there are differences among batches. Once again, both raw material characteristics and process conditions are fundamental in AA formation. Therefore, geographic location, product variety, possible inhibitors of browning reaction, thermal load of the process, seasonality and heat transfer (heat transfer mechanism), among others, must be considered.
22	Chilean Food Quality and Safety Agency (ACHIPIA)	Methods of analysis	Designs of standarized analytical technologies are proposed, besides technical validation to measure acrylamide through Certificate Material of Reference (CMR) and measures in different laboratories through intercomparison exercises. The recommended method HPLC – MS/MS is the most adequate according to our experience. However, it is proposed to search for faster and cheaper methods to measure AA. In line with this, there are other techniques to determine acrylamide in food, like Gas Chromatography–Mass Spectrometry (GC-MS) based technique. Last publications apparently confirm the validity of both techniques mentioned, which enables to guarantee the determination of acrylamide with quantification limits of 30 µg/kg through HPLC–MS–MS and 5 µg/kg with GC–MS–MS , using liquid-liquid extraction techniques. In addition, there are methods of analysis having QuEChERS (Quick, Easy, Cheap, Effective, Rugged and Safe), that is, extraction systems to obtain a very high recovery of the analyte of interest, in a rapid, safe and reproducible way. These would decrease the high uncertainty of the available extraction methods. It is suggested to put greater emphasis on the process of extraction since foods are very complex matrixes that change according to the type of preparation. This is reflected in the dispersion of results obtained in the contents of AA. It has been thus proved that the analyses in potato chips or biscuits are consistent, there are other matrixes like cocoa with more dispersion in the results. Foods with high levels of sugar present the highest limitation of the method. On the other hand, it is difficult to copy the experiment at domestic level and therefore, the experimental disturbances mask significant differences. The analysis carried out through a Chilean project is commented: FONDEF GC-MS, with no derivation of direct extraction with methanol and acetonitrile; clean-up by C18 reverse phase is used for products with high content of oil. Extraction technique depends on the type of matrix; extrapolations among matrixes affect negatively to recovery percentages and method sensibility. Through this method, limits similar to literature were obtained.
23	Chilean Food Quality and Safety Agency (ACHIPIA)	Occurrence and patterns of AA in	Many foods with high levels of AA must be emphasized in some countries with techniques to quantify them and

		food	estimate their consumption. The Information indicated is clear: highest levels of AA are found in potato chips and French fries along with coffee, followed by bakery products including rusks and biscuits; extruded cereals and baby food. However, the content of acrylamide in potato chips is clearly decreasing. The contents of AA found in foods were expected since they are the most susceptible to generate AA in their elaboration. The content of AA is heterogeneous among different food matrixes and into the matrix itself. On the other hand, the great variety of processed and homemade food show different levels of AA, as well as the food itself has different concentration due to its variability and preparation. The influence of diverse factors such as place, consumption habits and trademarks on the contaminant content is studied in the document. Differences up to 15% for potato chips in different trademarks prepared at standard environmental conditions were found. The "roasting grade" is difficult to quantify due to its high variability. It is recommended to standardize the "roasting level", for example, by using computer vision techniques. In addition, it is very important to revise the type of heat source used and define the conditions explicitly.
24	FoodDrinkEurope (FDE)	Food Description	From line 1197 -1212: For clarity it is important to use consistent terminology throughout the draft Scientific Opinion e.g. there should be a clear and consistent differentiation between 'French fries' and 'potato crisps'. The section 'Food Description' (page 32 onwards, lines 1197 onwards) already include detailed descriptions of the categories. However looking at the bulk of the draft Opinion the terms 'French fries/potato chips', 'potato chips' or 'chips', are frequently used, and therefore when reading the text it is not always clear to which type of product the authors are referring. A specific example is within the section on 'intake assessment' which includes the terms 'chips', 'potato chips' and 'hot chips' - all of which we presume in the context of the section most probably refer to 'French fries' (lines 2287, 2317, 2359, 2395, 2820). FoodDrinkEurope would suggest that where the term 'potato chips' is used within the text, extra care should be taken to clarify whether the reference is to 'Potato Crisps' or else to 'Potato Fried Products'. For clarity we would suggest that where 'Potato Fried Products' are referenced as a standalone category, they should be referenced as 'Potato Fried Products (except potato crisps and snacks)'. The definition be mentioned under this

			section.
25	FoodDrinkEurope (FDE)	Data submitted by European Countries	Lines 1243-1265: FoodDrinkEurope welcomes the recognition and inclusion of the occurrence data that was submitted by industry, comprising data from various sectors.
26	Kantonales Labor Zurich	Description of the occurrence levels	Underestimated AA formation in domestic kitchens and restaurant Exposure assessments tend to underestimate home-made foods. AA-data were mainly collected by enforcement authorities. They go to shops and collect food samples, perhaps preparing prefabricates according to the instructions in the laboratory. They do not go to the homes and look at what people prepare from raw foods (they are not competent for that). Frying left-overs do not show up in statistics. Products fried and roasted at home have scarcely been sampled. I doubt that the samples of "other potato fried products" reflect the full spectrum, particularly that the 12 samples of Rösti would fit to a mean value of 606 µg/kg AA and a maximum of 1549 µg/kg. This might explain the poor correlation between the estimated dietary exposure and internal biological markers mentioned in line 672. The probably most relevant domestically prepared food item is roasted potatoes, frequently consumed by a broad population in a large part of central Europe. There is little data, as the products are ill-defined and strongly vary. In Switzerland, Rösti (hash browns in the US) is the dominating source of AA for frequent eaters: brown Rösti, as often served in restaurants, contains 1000-5000 µg/kg AA. We did not produce random data fitting into the EFSA statistics, as a targeted investigation seemed more useful. The preparation of Rösti was optimized with the help of professional cooks from the School of Hotel Management Belvoirpark, Zurich, to produce a culinary good product with an AA content as low as possible. Under comparable roasting conditions, AA formation is approximately proportional to the content of reducing sugars. As a reference point, optimized Rösti of typical flavor and some crispiness prepared from potatoes containing 2.5 g/kg reducing sugar contained approximately 1000 µg/kg AA (see graphic below). Under less optimized conditions, such as faster roasting at higher temperature, it was 2000-3000 µg/kg [1]. Acrylamide contents in optimized Rösti depending on the content of reducing Freshly harvested potatoes (July to October) typically contained 0.3-3 g/kg reducing sugars (depending on variety [2]), but for the rest of the year, the marketed potatoes tend to be from cold storage and concentrations are in the range of 3-15 g/kg [3]. With these, AA-concentrations in optimized Rösti are in the range of 2000-5000 µg/kg. When sugars exceed around 5 g/kg, roasting must be stopped earlier, as the Rösti turns exceedingly dark and bitter otherwise, but this prevents crispiness. A single portion (250 g) of Rösti easily contains 500-1250 µg AA. Consumed every third day (I grew up this way)

			this results in an average AA exposure of 166-416 µg/d or 2.6- 6.9 µg/kg bw/d. A single serving of such Rösti contains approximately the amount of AA calculated in the draft opinion for all other foods during 10 d. 1 How much reducing sugar may potatoes contain to avoid excessive acrylamide formation during roasting and baking? S. Biedermann-Brem, A. Noti, K. Grob, D. Imhof, D. Bazzocco and A. Pfefferle. Eur. Food Res. Technol. 217 (2003) 369-373. 2 Potential of acrylamide formation, sugars and free asparagine in potatoes: a comparison of cultivars and farming systems. T. M. Amrein, S. Bachmann, A. Noti, M. Biedermann, M. Ferraz Barbosa, S. Biedermann-Brem, K. Grob, A. Keiser, P. Realini, F. Escher and R. Amadò. Journal of Agricultural and Food Chemistry 51 (2003) 5556-5560. 3 Acrylamide monitoring 2007-2009 in Switzerland: results and conclusions. M. Biedermann, F. Grundböck, K. Fiselier, S. Biedermann, Ch. Bürgi, and K. Grob. Food Additives Contaminants 27 (2010) 1352-1362.
27	FoodDrinkEurope (FDE)	Potato crisps and snacks	4.1.3.2. Potato crisps and snacks 1800 characters Lines 1404-1413: For clarity it is important to use consistent terminology throughout the draft Scientific Opinion e.g. there should be a clear and consistent differentiation between ‘French fries’ and ‘potato crisps’. The section ‘Food Description’ (page 32 onwards, lines 1197 onwards) already include detailed descriptions of the categories. However looking at the bulk of the draft Opinion the terms 'French fries/potato chips', 'potato chips' or 'chips', are frequently used, and therefore when reading the text it is not always clear to which type of product the authors are referring. A specific example is within the section on 'intake assessment' which includes the terms ‘chips’, ‘potato chips’ and ‘hot chips’ - all of which we presume in the context of the section most probably refer to ‘French fries’ (lines 2287, 2317, 2359, 2395, 2820). FoodDrinkEurope would suggest that where the term 'potato chips' is used within the text, extra care should be taken to clarify whether the reference is to 'Potato Crisps' or else to 'Potato Fried Products'. For clarity we would suggest that where ‘Potato Fried Products’ are referenced as a standalone category, they should be referenced as ‘Potato Fried Products (except potato crisps and snacks)’. The definition be mentioned under this section. Lines 2287, 2317, 2359, 2395, 2820: For clarity it is important to use consistent terminology throughout the draft

			Scientific Opinion e.g. there should be a clear and consistent differentiation between ‘French fries’ and ‘potato crisps’. The section ‘Food Description’ (page 32 onwards, lines 1197 onwards) already include detailed descriptions of the categories. However looking at the bulk of the draft Opinion the terms 'French fries/potato chips', 'potato chips' or 'chips', are frequently used, and therefore when reading the text it is not always clear to which type of product the authors are referring. A specific example is within the section on 'intake assessment' which includes the terms ‘chips’, ‘potato chips’ and ‘hot chips’ - all of which we presume in the context of the section most probably refer to ‘French fries’
28	FoodDrinkEurope (FDE)	Coffee and Coffee substitutes	Lines 1436 -1436: It is stated that ‘roasted coffee’ was found to be less contaminated than ‘instant coffee’ on basis of the analysis of the ‘dry (as sold)’ products. This is less relevant than the comparison of the levels in the products ‘as prepared for consumption’. When taking the averages (mean middle bound values: Roast coffee: 249 µg/kg; Instant coffee: 710 µg/kg) and the dilution factors ‘Roast coffee: 0.053; Instant Coffee: 0.017) the mean level for ‘as prepared for consumption’ for roast coffee is 13.2 µg/l respectively 12.1 µg/l for instant coffee. This leads to the conclusion that levels of acrylamide in both sub-categories are at a similar/ not significantly different level. Lines 1441-1445: On the comparison between ‘regular’ and ‘decaffeinated’ coffee: The comparison as included in the opinion is based on monitoring data and the regular and decaf subsets are not comparable due to different blends and roasting conditions. It is proposed to refer to the conclusion on the effect of decaffeination as included in the FoodDrinkEurope Toolbox: ‘Trials showed that roasting of decaffeinated green coffees (covering the commercially important decaffeination processes) resulted in AA levels of the same magnitude as roasting of corresponding untreated coffees when roasted under comparable roasting conditions.’
29	National Coffee Association USA (NCA)	Coffee and coffee substitutes	2. Description of occurrence levels/Coffee and coffee substitutes, line 1432-1448 The food category “coffee and coffee substitutes” is comprised of several subcategories with very different AA levels in the dry product. As shown in Table 6 (line 1359), the mean value for “roasted coffee (dry)” is 249 micrograms per kilogram (µg/kg), as compared to mean values of 710 µg/kg for “instant coffee (dry),” 510 µg/kg for “substitute coffee (dry), based on cereals,” 2,942 µg/kg for “substitute coffee (dry), based on chicory,” and 415 µg/kg for “substitute coffee (dry), unspecified.” These data clearly indicate that AA levels differ between these categories, particularly substitute coffee based on chicory. We recommend that “coffee” and “substitute coffee” be treated as separate food categories.

30	European Coffee Federation (ECF)	Coffee and coffee substitutes	Line 1435-1436: It is stated that 'roasted coffee' was found to be less contaminated than 'instant coffee' on basis of the analysis of the 'dry (as sold)' products. This is less relevant than the comparison of the levels in the products 'as prepared for consumption'. When taking the averages (mean middle bound values: Roast coffee: 249 µg/kg; Instant coffee: 710 µg/kg) and the dilution factors 'Roast coffee: 0.053; Instant Coffee: 0.017) the mean level for 'as prepared for consumption' for roast coffee is 13.2 µg/l respectively 12.1 µg/l for instant coffee. This leads to the conclusion that levels of acrylamide in both sub-categories are at a similar/ not significantly different level.
31	European Coffee Federation (ECF)	Coffee and coffee substitutes	line 1441-1445: On the comparison between 'regular' and 'decaffeinated' coffee: The comparison as included in the opinion is based on monitoring data and the regular and decaf subsets are not comparable due to different blends and roasting conditions. It is proposed to refer to the conclusion on the effect of decaffeination as included in the FoodDrinkEurope Toolbox: 'Trials showed that roasting of decaffeinated green coffees (covering the commercially important decaffeination processes) resulted in AA levels of the same magnitude as roasting of corresponding untreated coffees when roasted under comparable roasting conditions.'
32	FoodDrinkEurope (FDE)	Temporal trend analysis of AA occurrence data in certain food categories	Lines 1467-1468: There is reference made to the 2012 EFSA monitoring report to state that 'coffee and coffee substitutes' has showed increasing levels during the period from 2007 to 2010. When looking into the details of the report, this trend analysis is based on the data for instant coffee only and on a very small data base (e.g. only 15 samples for 2010). The trend analysis is driven by lower than realistic mean levels for 2007 and 2008. In addition, the small 2010 database is influenced by one single outlier with an extraordinary high acrylamide level. Industry data as provided to EFSA does not confirm a trend of increasing levels in instant coffees over time. We accordingly would like to have the reference to coffee removed in the statement of increased levels for the 2007 – 2010 period.
33	European Coffee Federation (ECF)	Temporal trend analysis of AA occurrence data in certain food categories	Line 1467-1468: There is reference made to the 2012 EFSA monitoring report to state that 'coffee and coffee substitutes' has showed increasing levels during the period from 2007 to 2010. When looking into the details of the report, this trend analysis is based on the data for instant coffee only and on a very small data base (e.g. only 15 samples for 2010). The trend analysis is driven by lower than realistic mean levels for 2007 and 2008. In addition, the small 2010 database is influenced by one single outlier with an extraordinary high acrylamide level. Industry data as provided to EFSA does not confirm a trend of increasing levels in instant coffees over time. We accordingly would

			like to have the reference to coffee removed in the statement of increased levels for the 2007 – 2010 period.
34	Spanish National Research Council (CSIC)	Impact of raw material and storage	Comments on lines 1663-1668: In June 2013, the Spanish National Research Council in collaboration with the Spanish Horticultural sector launched an investigation on the aptitude of fresh and stored potato under frying. Investigation aimed to clarify the impact of storage on the formation of acrylamide after frying*. It has been well stablished that asparagine, and, mainly, the reducing sugar content is the driving factor of acrylamide formation during thermal treatment of potato-based products. Sometimes consumers are not able to distinguish properly between fresh and stored potato tubers at the market. Nowadays, the technologies applied to the conservation of potato provide tubers with almost no external signals of senescence. However, the price on the market and seasonality of the stored product make it a product more affordable and attractive to consumers. In this investigation, there were selected a number of varieties of potato tuber (Agria, Caesar, Monalisa, Agata, and Bellini) which are marketed in Spanish. All the samples had a satisfactory visual acceptance by consumers. Strips (0.8 x 0.8 x 6 cm) of fresh and stored potatoes were fried in a domestic fryer (5L, 2200 watts) at 180ºC in two cycles of frying. Processes and numbers of samples allowed statistical analysis of the results. In addition a number of quality parameters (chemical and physical) were analyzed, including the acrylamide content. Results clearly show that levels of acrylamide were significantly higher in stored potatoes as compared with raw potatoes. For instance, Caesar variety (295 v.s. 2785 µg/kg), Monalisa (388 v.s. 4959 µg/kg), and Agata (476 v.s. 4072 µg/kg), being (raw v.s. stored). Levels of acrylamide in stored potato tubers were largely triggered at the beginning of the second cycle of frying. This investigation pointed out the importance to provide to consumers with clear information to select the most appropriate potato tuber for each cooking process. Fresh and stored potato tubers with similar external appearance and fried under the same conditions will produce significantly different levels of acrylamide being lower in fresh potatoes. * Full report (Spanish only) is available under request (fjmorales@ictan.csic.es)
35	FoodDrinkEurope (FDE)	Impact of raw material and storage	Lines 1467-1468: There is reference made to the 2012 EFSA monitoring report to state that ‘coffee and coffee substitutes’ has showed increasing levels during the period from 2007 to 2010. When looking into the details of the report, this trend analysis is based on the data for instant coffee only and on a very small data base (e.g. only 15 samples for 2010). The trend analysis is driven by lower than realistic mean levels for 2007 and 2008. In addition, the small 2010 database is influenced by one single outlier with an extraordinary high acrylamide level. Industry data as provided to EFSA does not confirm a trend of increasing levels in instant coffees over time. We accordingly would like to have the reference to coffee removed in the statement of increased levels for the 2007 – 2010 period.
36	Novozymes A/S	Impact of processing	Use of asparaginase for acrylamide mitigation has proven successful in a range of food products. The enzyme hydrolyses the precursor asparagine, hereby reducing final acrylamide formation. 4 asparaginase products are commercially available and widely used in e.g. biscuits and snacks in more than 30 countries. Commercial

			applications are also starting on potato granules and green coffee beans. Potatoes and potato based products Potato snacks Dough based potato snacks are typically made using dried potato flakes or granules. Adding the asparaginase directly to the dough showed 45 to 95% reduction in acrylamide formation in the final snack, depending on enzyme dosage and dough water content. Alternatively, enzyme pre-treated potato flakes or granules can be used. When tested in pilot scale using a mix of pre-treated potato granules and non-treated potato flakes, acrylamide concentrations in the final snack were reduced by 40%. French fries Asparaginase was tested in French fry production by dipping blanchedpotato strips in enzyme solution before drying. The time in the drier is exploited for enzyme action. Results in lab scale have shown 40-60% reduction in acrylamide levels depending upon enzyme dosage. Further testing in pilot scale confirmed these results. In full scale production the enzyme was applied directly to blanched potato strips using a coating system. Results showed a 43 to 53% drop in acrylamide levels. An improved asparaginase specifically for French fries is currently being developed. This will allow for a direct implementation of the enzyme into the production without any process changes, as is needed for the existing enzyme product. Cereals and cereal based products Biscuits and crackers The FoodDrinkEurope Acrylamide Toolbox reports that “use of asparaginase is effective in biscuits, cereals, crisp bread, and today is applied to commercial products”. For dough based cereal products the asparaginase is mixed in with other ingredients, and dough mixing and holding time used for the enzyme
37	FoodDrinkEurope (FDE)	Impact of processing	Potatoes and potato based products Lines 1728-1737: The summary for of the paper for Yuan et al 2014 the text states that the optimal soaking treatments could effectively reduce the AA content whilst reasonably retaining the sensory attributes of crisps. All such research is to be welcomed, and will doubtless be investigated by manufacturers for potential inclusion within the FoodDrinkEurope AA Toolbox. However, for a technique to be recommended as an effective mitigation tool the research requires evaluation within pilot plants or test runs within a factory to verify whether it delivers

			measurable reductions, and whether it can be applied successfully under commercial production conditions. Often, it is found that promising new research will have some risks to product attributes and/or inconsistent mitigation results when scaled up and applied within a commercial setting. In our initial view, it would appear that the technique as described would be impractical within current commercial settings, and we would also expect to see some major impacts upon the organoleptic properties of the final foodstuffs which the authors perhaps have not been able to consider. Given this uncertainty we would suggest that the text should be amended to read "The authors believe that optimal soaking treatments could effectively reduce the AA content while reasonably retaining the sensory attributes of the crisps."
38	Kantonales Labor Zürich	Impact of processing	Lines 1698-1703 refer to work from Matthäus on frying temperatures. I would like to point out that in these experiments the duration of frying was kept constant, which means that at higher temperature frying was more intensive. This is not practice-oriented: higher temperatures are used to shorten frying and, in fact, similar product properties (such as crispiness) are achieved in less time. Reality is even more complex, as the addition of the raw French fries to the oil strongly cools the oil and temperature only recovers towards the end of the process (depending on the amount of potato added and the power for the fryer). When considering this, dependence of temperature is weaker. In fact, clearly higher temperatures can be used in the beginning if temperature is then allowed to drop without increasing again to the initial values towards the critical last moments of frying [1]. One of the main producers of fryers confirmed feasibility, but he would only start making such fryers if there is a regulatory requirement ensuring sales. [1] Influence of the frying temperature on acrylamide formation in French fries. K. Fiselier, D. Bazzocco, F. Gama-Baumgartner, K. Grob. Eur. Food Res. Technol. 222 (2006) 414-419
39	Renaissance BioScience Corp.	Concluding remarks	Section 4.4.3 (lines 1788-1793): Impact of raw material, storage and processing on AA levels in food—Concluding remarks The use of Renaissance BioScience's acrylamide-preventing (AP) yeast technology circumvents the need for a variety of acrylamide control and reduction practices—involving a vast range of parameters and representing broad scale intervention—that are logistically and technically challenging, as well as extremely costly. The benefits of this yeast technology – which, aside from an accelerated ability to consume asparagine, is identical to parental Saccharomyces cerevisiae (baker's yeast) in every other way – can be realized by eliminating the need for expensive changes throughout the entire food production process, from growing and handling, through manufacturing and storage of food

			products. Upstream prevention of acrylamide formation through asparagine consumption afforded by Renaissance AP yeast obviates the need to control multiple parameters during rest of the food production process. This greatly simplifies the process of AA reduction, and is not affected by non-standardized downstream manipulations of food products.
40	Renaissance BioScience Corp.	Initiatives for mitigation measures	Section 4.5 (lines 1798-1817): Initiatives for mitigation measures. Renaissance BioScience (www.renaissancebioscience.com) has devoted five years of research to the discovery and painstaking classical development of a yeast that naturally consumes asparagine at an accelerated rate. This acrylamide-preventing yeast (or AP yeast), which is identical to parental Saccharomyces cerevisiae (baker's yeast) in every other way, not only virtually eliminates asparagine (and thus, the downstream formation of acrylamide), but also seamlessly and easily replaces baker's yeast in all baking processes, thereby solving the acrylamide problem in the final baked product. Our AP yeast can be reliably produced in the quantities required for food manufacturers, is in long-term testing with a large number of major food manufacturers and will be available for commercial sales in 2015. Its ease of use makes it ideal for any size food manufacturer or processor ranging down to the home kitchen, and will make it an invaluable addition to the AA reducing toolbox as a fast-emerging natural acrylamide-preventing food processing technology that food manufacturers will find efficient and reliable.
41	European Potato Processors' Association (EUPPA)	Initiatives for mitigation measures	EUPPA (European Potato Processors' Association) thanks EFSA for the public consultation on its draft Scientific Opinion on acrylamide in Food. EUPPA supports the development of evidenced-based public health policy, underpinned by robust science and welcomes the call for further diet studies to improve risk assessment. The industry is committed to ensuring that acrylamide in food is kept as low as reasonably practicable and will continue to support the monitoring and reporting of acrylamide occurrence data. Since the beginning, the European potato industry has contributed to development of tools (Food Drink Europe Toolbox, pamphlets, goodfries.eu website, training webinars, etc.) and will continue efforts to mitigate acrylamide in potato products. To help consumers to prepare products in home to acceptable levels the industry has modified the cooking recommendations on product packaging as of 2004 to clarify the method to achieve an optimal sensory quality while limiting the potential formation of acrylamide in the cooked product. Furthermore, EUPPA set up a website www.goodfries.eu in 28 languages, which provides crucial information on how to prepare potato fries in a healthy way. The website contains an instruction video, as well as printable instructions, which can be placed in both

			professional and domestic kitchens. EUPPA will continue its active contribution to Food Drink Europe works, in partnership with EFSA, the European Commission and Member States to reduce consumer exposure to acrylamide in food. EUPPA is also working with its supply chain partners to achieve the best results.
42	FoodDrinkEurope (FDE)	Initiatives for mitigation measures	Lines 1794-1873 371 characters Line 1818 states "In addition to the AA toolbox, FoodDrinkEurope, in close co-operation with the European 1819 Commission and national authorities, has published pamphlets in 22 European languages". In fact these pamphlets are currently available in 23 European languages (Norwegian translations being added in 2011). In addition Croatian language translations of the pamphlets are currently awaiting publication.
43	Kantonales Labor Zürich	Initiatives for mitigation measures	Section 4.5 on mitigation should be completed by successful measures which underline that improvements are feasible, such as those in Switzerland with regard to potato products. Use of asparaginase is another successful measure that was not adequately addressed. French fries For “industrial” potatoes, i.e. those intended for prefabricates such as French fries, Rösti, and croquettes, Swisspatat (controlling the Swiss trade of potatoes; [1]) sets a minimum quality defined (among other parameters) by a frying test (browning after standardized frying). Calibrated in terms of reducing sugars this minimum corresponded to 0.76 g/kg fructose + glucose [2]. An exception with a far lower baking note is made for the one potato variety (Innovator) that is used for the international fast food chains: these insisted in selling “Western style” French fries with stronger browning. In the Swiss monitoring 2007-2009, the mean concentration in the French fries prefabricated for the normal Swiss market was 0.35 g/kg (n=92) while that for the “Western style” French fries was 1.38 g/kg (n=38) [3]. Already in 2004 the AA concentrations in “normal” French fries sold in restaurants was usually between 50-100 µg/kg [4,5], in the monitoring 2007-2009 the mean concentration was 84 µg/kg, which is far below the values mentioned in the draft opinion. In the same period, the mean AA concentration in the “Western style” French fries was 345 µg/kg. In fact, as easily noticed, “normal” French fries in Swiss restaurants are less brown than elsewhere – and nobody complains. Switzerland hardly imports potatoes, in particular none from warmer countries in late spring for producing French fries, which means that tubers are stored up to the next harvest. This demonstrates the feasibility of substantial improvement: it is the proof that French fries with less than 100 µg/kg

			AA can be produced in practice and that the indicative value in Commission Recommendation 2013/647/EU(600 µg/kg) is far too high if health concerns are taken serious. Potatoes Rösti, hash browns, Bratkartoffeln and similar products are easily the far dominating source of exposure to AA for some consumers. As the reducing sugars had been too high during most of the year (storage at 4 °C), in 2004 a separate line of tubers intended for these critical applications were introduced: tubers of suitable varieties are stored at about 8-9 °C to prevent liberation of reducing sugars and sold by the retail market (even by German retailers – which do not offer this on their home market). Concentrations of reducing sugars are, in fact, substantially lower [3]. [1] http://www.kartoffel.ch/fileadmin/branchenecke/Mitteilungen/Produzente_DE/August_13/UB13_d.pdf [2] Acrylamide: Swiss frying test instead of measuring reducing sugars to evaluate potatoes for frying and roasting? R. Mini, K. Fiselier and K. Grob. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 95 (2004) 477-488 [3] Acrylamide monitoring 2007-2009 in Switzerland: results and conclusions. M. Biedermann, F. Grundböck, K. Fiselier, S. Biedermann, Ch. Bürgi, and K. Grob. Food Additives Contaminants 27 (2010) 1352-1362 [4] Good manufacturing practice (GMP) for French fries low in acrylamide: results of a pilot Project. K. Fiselier, F. Gama-Baumgartner, A. Fiscalini, M. Biedermann, K. Grob, D. Imhof and M. Beer. Mitteilungen aus Lebensmitteluntersuchung und Hygiene 95 (2004) 127-134 [5] French fries with less than 100 µg/kg acrylamide. A collaboration between cooks and analysts. K. Grob, M. Biedermann, S. Biedermann-Brem, A. Noti, D. Imhof, Th. Amrein, A. Pfefferle, D. Bazzocco. Eur. Food Res. Technol. 217 (2003) 185-194
44	Frozen Potato Products Institute (FPPI)	Initiatives for mitigation measures	As a trade association representing the producers and processors of frozen potato products, the Frozen Potato Products Institute (FPPI) respectfully submits the following comments to the EFSA Panel on Contaminants in the Food Chain regarding the draft Scientific Opinion on Acrylamide in Food. • Section 4.5 (Line 1794): It is important that risk-benefit tradeoffs be considered when considering specific mitigation strategies. The Codex Alimentarius Code of Practice recognizes this principle, explaining that "[m]easures aimed at reducing levels of acrylamide cannot be taken in isolation from other considerations." According to the Code of Practice, "[p]recautions need to be taken to avoid compromising the existing chemical and microbiological safety of the food" and to ensure the "nutritional qualities of products… remain unimpaired." Some of the mitigation measures have been proven difficult to translate from the laboratory bench to the manufacturing facility floor. FPPI

			recommends that EFSA incorporate this important principle from Codex into the scientific opinion.
45	Association of the German Confectionery Industry (BDSI)	Initiatives for mitigation measures	Pease insert on page 52/53 (section 4.5. Initiatives for mitigation measures) from Line 1824 the red marked text: *In* *Germany, a concept of minimising AA concentrations in foodstuffs was already introduced in 2002 (Göbel and Kliemant, 2007). Foodstuffs analysed within official food control were compiled and classified into certain food groups. Those foods which make up the 10 % most contaminated products in each group were identified. The lowest of the AA contents of these upper 10 % is the so-called „signal value" for this group. If the signal value is higher than 1 000 µg/kg, the signal value will automatically be 1 000 µg/kg. Additionally, an observation of single products stemming from producers with an important market position was performed. If AA concentrations were found above the signal value, the competent authorities contacted the respective food producer and entered into the minimisation dialogue to check whether ingredients or processes could be changed to minimise AA contents, and which changes this could be. The signal values were updated annually by the German Federal Office for Consumer Protection and Food Safety (BVL). Once calculated, signal values were not raised as long as this minimisation concept was pursued, but were maintained or lowered. This means that AA contents in relevant foods will be continually reduced if the minimisation measures are successful. Food with AA contents of more than 1 000 µg/kg and from food groups for which no signal values have been set will automatically be included in the minimisation dialogue described above.* The far-reaching successes of the minimisation efforts undertaken in Germany are documented by the continuously lowered signal values (Raters, Matissek 2012). *The German national minimising concept with the calculation of signal values was widely replaced in 2011 with the introduction of EU wide indicative values.* *In 2009, BVL summarized the AA concentrations which formed the basis for the calculation of the German signal values in order to explore the effectiveness of the mitigation measures. While the decrease of the mean AA concentrations in potato chips pointed to a successful application of the toolbox by food industry during the standardized industrial production of this potato product in the observed time span, the course of the mean AA concentration in French fries and potato patties showed either a stagnation or considerable variation. This may be partly due to the inclusion of samples from households and small snack-bars with no standardized food preparation.* The effectiveness of the minimisation measures implemented in potato crisp production in Germany since April 2002 is documented by the regularly updated weekly mean values (Raters, Matissek 2012) 33. *A similar variation of the mean AA concentration over time was seen for gingerbread, a traditional spicy Christmas cookie and crispbread, which is probably due to the use of different traditional recipies and manufacturing processes, often in small bakeries, that are not applying the same effective mitigation measures as the bigger food industries.* In the footnote at the end of page 53 the following must be added: 33 http://www.lci-koeln.de/deutsch/verbraucherinformation-zur-thematik-acrylamid-bei-kartoffelchips

			In the Reference-List the following must be added: Raters M, Matissek R (2012) 10 Jahre Acrylamid ─ Rückblick und Status quo. Deut Lebensm-Rdsch 108: 184-189
46	Chilean Food Quality and Safety Agency (ACHIPIA)	Food consumption	The food consumption data base in Europe is fundamental, specifically regarding the type of food and its consumption according to the age group. It is important, however, to specify the type of food, its elaboration and preparation. There is a lot of information in this regard by consumption surveys, but there are differences in the data, since natural variables concerning raw materials, additives, mitigation processes, industrial or home processing, storage, affect the results. The AA content can have significant variations in the same food processed by different companies or in batches of the same food produced by the same company (Chilean data).
47	FoodDrinkEurope (FDE)	Food consumption	Line 1860: Spelling of "recipes" (currently reads “recipies") Line 1902: The term ‘coffee Americano’ is not a common term across Europe. We would propose to replace it with ‘drip filter coffee’.
48	Frozen Potato Products Institute (FPPI)	EFSA’s Comprehensive European Food Consumption Database	As a trade association representing the producers and processors of frozen potato products, the Frozen Potato Products Institute (FPPI) respectfully submits the following comments to the EFSA Panel on Contaminants in the Food Chain regarding the draft Scientific Opinion on Acrylamide in Food. Section 5.1 (Line 1889): In determining the consumer intake of fried potato products, EFSA relied on some consumer surveys that assume if during a same meal both potato and oil or fat for frying were consumed, and the oil/fat represented more than 5% of the total consumption of potato and oil/fat, the potato was fried. This assumption may greatly overestimate the actual consumer intake of fried potato products. According to the United States National Nutrient Database for Standard Reference (Release 27) (http://ndb.nal.usda.gov/) published by the United States Department of Agriculture, French fries sold in restaurants typically contains more than 10% oil/fat. Moreover, the same database also reports that potato salad, which contains both potatoes that are usually boiled and oil/fat, has more than 5% oil/fat of the total consumption of potato and oil/fat. FPPI recommends that EFSA reconsider whether 5% is the proper cut-off for assuming the potato was fried in consumer surveys.
49	European Coffee Federation (ECF)	EFSA’s Comprehensive European Food Consumption Database	line 1902: The term ‘coffee Americano’ is not a common term across Europe. We would propose to replace it with ‘drip filter coffee’.

50	Chilean Food Quality and Safety Agency (ACHIPIA)	Human exposure assessment	The exposure assessment was based on total diet studies through reminder surveys (24-48 hours), considering only those people who replied for more than 2 days, so as to base the study on chronic users. As set forth, Europe is considered to have a good data base, since studies from 17 countries from 2000 to 2012 could be collected. However, a single estimation for European population is not possible due to disparity in the data. In addition, the determination of exposure to AA was based on a specific group of foods, through the analysis of each one of them. This can be a weakness due to an overestimation of the exposure to AA, because it is not considered as total diet. It is of concern that children, infants and babies are the most exposed groups to dietary acrylamide, probably because of acrylamide levels in breakfast cereals, potato chips and snacks, their frequency of consume and dietary habits.
51	Anonymous	Human exposure assessment	Jecfa calculated 1.0 resp. 4.0 µg/kg bw/d in 2005 and did the same in 2010 because "*neither the estimated average acrylamide exposure for the general population … nor the exposure for consumers with high dietary exposure … had changed*" (JECFA, 2010: 7). In 2014 EFSA summarized the results of the monitoring period from 2007 to 2010, concluded that "the trend analysis did not show any major changes in AA levels" (EFSA, 2014: 43, 1465) and calculated an exposition of 0.5 resp. 1.0 µg/kg bw/d. The BfR updated its exposure assessment in 2011, also based on monitoring data. The result was a average exposure of 0.14 and a high exposure of 0.39 µg/kg bw/d. These values were so low that BfR assumed that the German data probably did not cover all foods which contain acrylamide and calculated the MOE on the basis of exposure data from a biomarker study (BfR, 2011). It is surprising that the German monitoring data does not cover all relevant foods. It is also surprising that the data quality is so poor on the European level. DG Sanco started its database already in 2002 (IRMM, 2006). In 2007 the Commission published guide-lines about the data to be delivered (EC, 2007). In 2014 EFSA finally states "that a reli-able Europe-wide temporal trend analysis is not feasible" (EFSA, 2014: 43, 1460) and suggests – after twelve years of acrylamide in food – a longer monitoring period. The exposure assessments differ considerably. They are based on weak monitoring data. Furthermore it is questionable whether it is appropriate to calculate the exposition by multiplication of monitoring data by food consumption data. Many European food safe-ty authorities as well as FDA and Health Canada launched exposure assessments in the course of time. Hardly anybody published the complete data, i.e. portion size and moni-toring data for each product, which makes the exposure assessments comprehensible. In 2002 the NFCA calculated the exposure of high consumers on the basis of a portion of 30 g French fries per day (NFCA, 2002), while BgVV estimated 236 g for one portion of ready-to-eat French fries (BgVV, 2002 b). If you combine both figures you get the result that the average high consumer eats one portion French fries per week. In Germa-ny 6.5 Million working people have lunch in 10,000 canteens, and their favorite dish are French fries (Gerber, 2010). One can assume that a lot of German people

			eat more French Fries than the average high consumer. Mestdagh et al. (2007) chose a method closely connected to real life when they measured the exposure of people who had lunch at a canteen. The exposure after one meal was 0.4 µg/kg bw/d, i.e. nearly as high as the average exposure according to EFSA in total should be. Another aspect which leads to low exposure assessments is the way to determine what a high consumer is. Those who consume high amounts of a product are not necessarily the most exposed consumers. According to the EFSA monitoring data 2010 the maximum level in French fries was 2,174 µg/kg, while the median level was 240 µg/kg (EFSA, 2012: 21). If somebody eats one portion of highly contaminated French fries, he/she consumes 510 µg acrylamide. The same person could have nearly ten portions of moderate contaminated French fries before reaching the same level of exposure. Conclusion and References follow in a separate comment (Please read my comment as a whole. I sent it via E-Mail)
52	Anonymous	Human exposure assessment	Conclusion: The exposure was calculated very differently by Jecfa and EFSA. Both agencies do agree that there is no evidence that the exposure did significantly change over the course of time. In this context the consumer had to learn that the agencies had not been able to collect data that was appropriate to create a trend-analysis. Many food authorities and many researchers calculated the public exposure. The underlying methods led to low results. => Hardly any benefits for the consumers: Food all over the world contains acrylamide, and even if the exposure is calculated on a low level, the difference between the human exposure and the dosis which leads to cancer in experimental animals is small. This was known very early on. There is no reason for the exposure to be exactly determined. Bet-ter answers will not be found as long as better methods are not available. References: – BfR - Bundesinstitut für Risikobewertung, 2011: Acrylamid in Lebensmitteln. Stellung-nahme Nr. 043/2011 des BfR vom 29. Juni 2011 [Acrylamide in Food. BfR Statement No. 043/2011, 06-29-2011]. In: http://www.bfr.bund.de/de/a-z_index/acrylamid-4185.html#fragment-2, accessed September 2014 – BgVV - Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin, 2002: Einfluss der Ernährung auf die Aufnahme von Acrylamid. Durch Änderungen im Ernährungs¬verhalten kann der Verbraucher die Acrylamid-Aufnahme deutlich reduzie-ren. Stellungnahme des BgVV vom 04.06.2002 [Influence of the diet on acrylamide exposure: The consumer can reduce the exposure by changing his eating behaviour. BgVV statement, 2002-06-04]. In: http://www.bfr.bund.de/cd/3862?index=65&index_id=4185, accessed September

			2014 – EC - European Commission, 2007: Commission Recommendation of 3 May 2007 on the monitoring of acrylamide levels in food (notified under document number C(2007) 1873). Official Journal of the European Union. L 123/33, (2007/331/EG). In: http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2007:123:0033:0040:EN:PDF, ac-cessed September 2014 – EFSA - European Food Safety Authority, 2012: Update on acrylamide levels in food from monitoring years 2007 to 2010, The EFSA Journal, Vol. 10, Issue 10, 2938-2975. In: http://www.efsa.europa.eu/en/efsajournal/pub/2938.htm, accessed September 2014 – Gerber, Maria, 2010: Das essen die Deutschen [What the Germans eat]. Die Welt, 2010-10-15. In: http://www.welt.de/print/die_welt/wissen/article10308549/Das-essen-die-Deutschen.html, accessed September 2014 – IRMM - Institute for Reference Materials and Measurements, 2006: Evaluated Data. Status June 2006. Preface. In: https://irmm.jrc.ec.europa.eu/activities/acrylamide/Pages/database.aspx, accessed September 2014 – JECFA - Joint FAO/WHO Expert Committee on Food Additives, 2010: Seventy-second meeting, Rome, 16–25 February 2010. In: http://www.who.int/foodsafety/chem/summary72_rev.pdf, accessed September 2014 – Mestdagh, Frédéric/Lachat, Carl/Baert, Katleen/Moons, Emmanuelle/Kolsteren, Pat-rick/Van Peteghem, Carlos & De Meulenaer, Bruno: Importance of a canteen lunch on the dietary intake of acrylamide. In: Molecular Nutrition & Food Research, Vol. 51, Issue 5, 509-516 – NFCA - Norwegian Food Control Authority, 2002: Risk Assessment of acrylamide in-take from foods with special emphasis on cancer risk. Report from the Scientific Com-mittee of the Norwegian Food Control Authority, 6 June 2002. In: http://www.mattilsynet.no/mat/mattrygghet/prosessfremkalte_stoffer/akrylamid/akrylamid_i_matvarer__norske_analyser_bekrefter_svenske_og_engelske_unders_kelser_3456, ac-cessed 28.11.2008
53	Kantonales Labor Zurich	Methodology	Scenarios: Exposure estimates should go into two directions: (i) population-oriented estimates (as presented in the draft opinion) to conclude that the MOE indicates a concern; (ii) exposure modeled by scenarios of consumer habits (combinations of food consumption with estimated AA-concentrations). Scenarios enable the detection of extreme exposures that are missed by statistical approaches. Even if only, e.g., 1 % of the population practices a given scenario, this relates to a large number of humans. Furthermore, scenarios yield data to set priorities and show which measure could help which consumers in reducing his/her exposure. They also enable determining the limits up to

			which given measures may reduce exposure, perhaps concluding that certain practices should be avoided. The BfR has done this at an early time, I did this later on [1]. In the present draft the modeling approach is not even addressed, even though important additional conclusions could be drawn – in particular it must be assumed that for some consumers exposure is markedly higher than now assessed. [1] Options for legal measures to reduce acrylamide contents in the most relevant foods. K. Grob. Food Additives and Contaminants 24 (2007) 71-81
54	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Food grouping	The use of the scenario modelling is appropriate but the base-line scenario is not sufficiently explained.
55	European Coffee Federation (ECF)	Food grouping	Line 2003: The term 'coffee americano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'.
56	European Coffee Federation (ECF)	Food grouping	Line 2006-2008: The dilution factor used to recalculate from coffee substitutes (solids) to coffee substitutes (beverage) is 0.125. This is not in accordance with actual market practice and advices for product preparation. The dilution factor should be 0.02. (More specifically, the dilution factor of 0.02 only applies to 'as sold' soluble coffee substitute products and a different factor in the same magnitude as the dilution factor for drip filter coffee should be taken for 'as sold' roast & ground coffee substitute products).
57	FoodDrinkEurope (FDE)	Food grouping	Line 2003: The term 'coffee americano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'. Lines 2006-2008: The dilution factor used to recalculate from coffee substitutes (solids) to coffee substitutes (beverage) is 0.125. This is not in accordance with actual market practice and advices for product preparation. The dilution factor should be 0.02. (More specifically, the dilution factor of 0.02 only applies to 'as sold' soluble coffee substitute products and a different factor in the same magnitude as the dilution factor for drip filter coffee should be taken for 'as sold' roast & ground coffee substitute products).
58	The Royal Belgian Association of the Biscuit,	Food grouping	Subject : Use of the gingerbread and lebkuchen data as AA value for speculaas in the exposure scenario

	Chocolate, Pralines and Confectionary (Choprabisco)		**Chapter/Section :**  Line nrs: line 1997 – 199 on page 57 and line 9344 on page 240 In Table D1 (page 240) the occurrence data of food category 6.4 (Gingerbread and Lebkuchen data - 407 µg/kg - are used for speculaas in the baseline exposure scenario. This does not correspond to the real occurrence data for speculaas since 2010. In our opinion it is more appropriate to use the occurrence data of food category 6.3 (Biscuits and wafers) : 201 µg/kg. Speculaas is a biscuit and the composition and processing are not comparable to the composition of gingerbread or lebkuchen. For speculaas the AA value decreased significantly between 2007 and 2012 by using mitigation tools. Data for countries with a significant consumption of speculaas: Germany: The Bfr reported: a decrease from 356 µg in 2005 to 163 µg/kg in 2010 (page 43 in the linked report) http://www.bfr.bund.de/cm/343/acrylamid-in-lebensmitteln.pdf Belgium: Measured by Belgian authorities: Period 2002 – 2007: n = 17 mean AA content: 346 µg/kg http://www.afsca.be/scientificcommittee/advices/_documents/Advice25-2008.pdf Period 2009 – 2013 : n = 8 mean AA content 283 µg/kg Comment on the 2009 – 2013 figures: The sampling might have been oriented to selective sampling , due to frequent exchange of information between CHOPRABISCO (The Royal Belgian Association of the Biscuit, Chocolate, Pralines and Confectionary) and the Belgian authorities on mitigation results. CHOPRABISCO A survey in 2014 showed that the mean AA value of speculaas consumed in Belgium is < 200 µg/kg France: Most of the speculoos consumed in France is produced in Belgium A survey in 2014 by CHOPRABISCO showed that the mean AA value of speculaas consumed in France is < 200 µg/kg
59	Austrian Agency for Health and Food Safety (AGES)	Left-censorship management	Line 2047: Regarding the left-censored management, why does EFSA refer to the WHO guidelines (GEMS/Food-EURO, 1995) and not to the EFSA document (Guidance of the Scientific Committee on a request from EFSA related to Uncertainties in Dietary Exposure Assessment, w006)?

60	Austrian Agency for Health and Food Safety (AGES)	Exposure calculation	Line 2055: Adding of "resulting in a distribution of exposure" → "..consumption for each food with the corresponding mean contamination, resulting in a distribution of exposure, summing up the respective…"
61	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	AA exposure levels across the different population groups	The exposure estimates in Table 8 appear very similar and it is not possible to determine if the levels are really different. Members asked if it was possible to comment on the uncertainties around the means.
62	Austrian Agency for Health and Food Safety (AGES)	AA exposure levels across the different population groups	Line 2078: According to AA-exposure, only the Lower Bound - and the Upper Bound-approach are used. Why not the Medium Bound (MB)? In the lines 2047-2050 the MB approach is also mentioned.
63	FoodDrinkEurope (FDE)	Food contributing to the total AA exposure	Lines 2066-2130: We would suggest the section on exposure is very interesting and useful to readers. % contributions to intakes are highlighted for some groups and some products on page 60. However, this is an incomplete and selective summary, making it difficult to read. It would be very useful to provide a full report of the actual % contributions to exposure for each food group and each population category.
64	FoodDrinkEurope (FDE)	Brand loyalty	Lines 2220-2259: The calculations performed here do not appear to be about loyalty to a particular brand, but loyalty to a particular product category under the terminology "potato crisps". Our understanding is that the analysis compares intakes calculated on the basis that all potato crisps consumed are "made from fresh potatoes through continuous process", with intakes calculated assuming all potato crisps that are consumed are "made from potato dough". "Brand" does not appear to play any role here. This would also appear to be the same with the coffee intake calculations. We would suggest that the title of this section needs to more closely reflect the calculations that have been undertaken e.g. Loyalty to particular product sub-type or category. This would also require amendment within the Summary.

65	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Potential non-dietary sources of exposure	This section could be expanded, and should include quantitative data on other sources wherever possible (or note when this is not possible) which would allow for a better understanding of the contribution of dietary exposure and would aid in interpreting the epidemiological studies and risk characterisation. This particularly relates to quantification of acrylamide exposures in smokers and also from environmental tobacco smoke. Data from studies that have measured haemoglobin adducts as an index of internal dose may be particularly helpful in this regard, but other analytical approaches could also be useful (e.g. estimation of inhaled doses, given measured concentrations in the air of workplaces).
66	FoodDrinkEurope (FDE)	Hazard identification and characterisation	Line2460 onwards: Clarity of the text on hazard identification and characterisation. In the section on hazard identification and characterisation (page 72 onwards) numerous studies are reviewed by CONTAM Panel and their conclusions are summarised. The conclusions and discussions of the CONTAM Panel are then presented. However the Panel's conclusions and discussions frequently appear within the body text rather than as a distinct numbered subsection. This format means that it is, in some instances, difficult to read and digest the information that is being presented. 7.3.5.2. Developmental toxicity Line 5532: Spelling "from" (currently reads "form")- Additional scientific papers for consideration by the EFSA CONTAM Panel. Recognising that the draft Scientific Opinion is based upon scientific papers available in open literature until May 2014, we note that subsequent to this date there have been a number of scientific papers in final publication which may be of relevance and could be considered by the EFSA CONTAM Panel. Whilst not intended to be a comprehensive list of new publications these papers include: – Dietary Acrylamide and Human Cancer: A Systematic Review of Literature. Nutr Cancer. 2014 Jul;66(5):774-90. doi: 10.1080/01635581.2014.916323. Epub 2014 May 29. Virk-Baker et al. – Dietary intake of acrylamide and esophageal cancer risk in the European Prospective Investigation into Cancer and Nutrition. Cancer Causes Control. 2014 May;25(5):639-46. doi: 10.1007/s10552-014-0359-5. Epub 2014 Feb 16. Lujan-Barroso L et al – Risk assessment, formation, and mitigation of dietary acrylamide: Current status and future prospects. Food Chem

			Toxicol. 2014 Jul;69C:1-12. doi: 10.1016/j.fct.2014.03.037. Epub 2014 Apr 5.Xu Y et al – Dietary intake of acrylamide and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition cohort. Obon-Santacana M eta l Br J Cancer 2014 Jun 17. doi: 10.1038/bjc.2014.328. Epub – Dietary acrylamide intake and the risk of colorectal cancer with specific mutations in KRAS and APC. Hogervorst JG et al Carcinogenesis 2014 May;35(5):1032-8. doi: 10.1093/carcin/bgu002. Epub 2014 Jan 7.
67	Frozen Potato Products Institute (FPPI)	Hazard identification and characterisation	As a trade association representing the producers and processors of frozen potato products, the Frozen Potato Products Institute (FPPI) respectfully submits the following comments to the EFSA Panel on Contaminants in the Food Chain regarding the draft Scientific Opinion on Acrylamide in Food. • Section 7.4.1.2.6 (Line 6583) There is no conclusive scientific evidence that support a relationship between dietary acrylamide intakes and increased risk of cancer. EFSA references Lipworth et al., 2012 to support its position in the scientific opinion that the current review papers did not provide a quantification of cancer risk. FPPI recommends that EFSA incorporate the entire conclusion of Lipworth et al., 2012 - "we found no consistent or credible evidence that dietary acrylamide increases the risk of any type of cancer in humans… In particular, the collective evidence suggests that a high level of dietary acrylamide intake is not a risk factor for breast, endometrial, or ovarian cancers… In conclusion, epidemiological studies of dietary acrylamide intake have failed to demonstrate an increased risk of cancer…" • Section 7.5.2 (Line 6935) In calculating the margin of exposure, EFSA used the carcinogenic data developed with the Harderian gland of rodent. As humans do not have Harderian gland, the relevance of using this endpoint to translate carcinogenic potential to humans is highly suspect. Although the metabolism pathways of acrylamide are similar in rats and humans, there might be significant quantitative differences in terms of sensitivity for different species. Additionally, for these types of assessments, it seems more appropriate to use the BMDL10 values based on rodent mesothelioma or sarcomas models listed in Table 28 to develop a margin of exposure. FPPI recommends that EFSA reconsider whether the risk assessment should be based on the BMDL10 value derived from the Harderian gland of rodent. As discussed above, given the uncertainties in the acrylamide dietary exposure and the evolving state of understanding of acrylamide toxicity, FPPI encourages EFSA to ensure that the final scientific opinion make it clear that there is no conclusive evidence that acrylamide presents any human safety concern at the current levels of dietary exposure.

68	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Toxicokinetics	Greater consideration could be given to potential impact of CYP2E1 being polymorphic in humans, highly inducible by alcohol, and expressed in Clara cells. It is recommended that a detailed analysis be made of kinetic differences between the inhalation and oral routes in humans, and also between human and animal exposures to investigate further the differences in susceptibility to tumours between species and following different routes of exposure.
69	Anonymous	Absorption and distribution	We suggest adding the following text to the section on Placental transfer, p. 76, l. 2629: "*Similarly, in a study, which included 1,101 cord blood samples and 172 maternal blood samples from Greece, Spain, England, Denmark and Norway (Pedersen et al. 2012), the median acrylamide Hb adduct levels in cord blood were approximately half of the levels in paired maternal blood. Hb adduct levels in cord blood were positively correlated with both maternal acrylamide (r = 0.95) and glycidamide Hb adducts (r = 0.94).*" Please add the following text to the section on Placental transfer, p. 77, l.2632 after von Stedingk et al. (2011): "*and Pedersen et al. (2012)*" Please add the following text to the section on Human studies, p. 97, l.3501: "*Likewise in the study which included 1,101 cord blood samples from Greece, Spain, England, Denmark and Norway (Pedersen et al. 2012), the median acrylamide Hb adduct levels were higher in cord blood from children of mothers who smoked (n = 129) than in children of nonsmokers (n = 972; 30.5 vs. 13.8 pmol/g Hb, p < 0.001). Corresponding levels for glycidamide adducts were 20.7 versus 10.1 pmol/g Hb (p < 0.001). Detailed information on maternal diet during pregnancy was obtained from the mothers using FFQs collected before or at the time of delivery and maternal intake of food and drink items known to contain potentially high levels of acrylamide (i.e. fried potatoes, potato chips, breakfast cereals, crisp bread, coffee, cookies, fine bakery products, bread and toast) were evaluated using an acrylamide food score for nonsmokers. A 1-unit increase in the acrylamide-rich food score was associated with higher Hb cord blood adduct levels for acrylamide (0.68 pmol/g Hb; 95% CI: 0.30, 1.06) and glycidamide (0.39 pmol/g Hb; 95% CI: 0.15, 0.63). In addition to dietary intake of acrylamide, the authors acknowledge that it is possible that acrylamide adducts were acting as a proxy marker for another dietary exposure or mix of exposures that were responsible for the associations observed, such as other Maillard reaction products that, like acrylamide, are formed during processing of food at high temperatures. Alternatively, acrylamide adducts may have been acting as a marker of a less healthy diet in general. Acrylamide may also be one of many contributors to the observed association. Adjusting for indicators of healthy and unhealthy eating habits (such as fruits and vegetables, fish, and soft drinks), maternal BMI, and indicators of socioeconomic status, did not substantially alter associations.*"
70	Joint submission by the UK Committee on Toxicity	Studies in mice	The COC agreed that the Harderian gland was an appropriate tumour to use for the BMDL derivations. Whilst not

	(COT) and UK Committee on Carcinogenicity (COC)		present in humans, it was well established that tumours in this gland were typically associated with genotoxic carcinogens and therefore it was difficult to exclude them from an assessment of carcinogenic potential. However, it was not clear from Appendix K why the Harderian gland had been selected, as lower BMDL values were obtained for mammary gland fibroadenomas in rats, which appeared to be equally appropriate to use. It was recommended that more clarification should be given about the choice of BMDL.
71	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	Overall, in this section I recommend to clearly separate the older studies (i.e., those performed before the JECFA assessment in 2005) from the more recent studies: for instance, it is unclear why (Zenick et al., 1986) is currently reported at lines 5240-2 amidst studies published in 2012-13. For older studies a short, general description might be sufficient. Conversely the section should concentrate on describing and discussing more recent studies, that are, in fact, thise providing more reliable and accurate information
72	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	General comment: There are evidence that immature animals are more sensitive to AA testicular effects compared to adults (see e.g., Takahashi et al., 2011, and also Koyama et al. 2011a, in the genotoxicity section). Moreover, the opinion identifies AA as a potential developmental toxicant. Therefore, a remarkable gap is the lack of a up-to-date extended one-generation or two-generation study in order to assess the effects on reproductive development and maturation upon pre- and post-natal continuous exposure. The only available study seems that by Tyl et al. (2000a): as it is reported (lines 5319-29 in the ensuing section 7.3.5.2. “developmental toxicity”) this study only investigated gross endpoints of reproductive “performance” (e.g., number of implantations and live pups) and apparently it does not meet current standards. The lack of up-to-date one- or two-generation studies investigating the AA effects on reproductive (especially male) development should, thus, be noted in the Opinion.
73	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	Lines 5254-5269: GA study (NTP, 2013, draft report): it is not clear the correspondence between the GA dose level and the AA intake that may produce that internal GA exposure. The whole opinion is based on risk assessment of AA exposure; thus such information would be useful to assess the possible relevance of this data for the characterization of reproductive hazards
74	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	Lines 5270-87: It is not clear the basis to derive the proposed reproductive NOAEL of 2 mg/kg.

			The study by Tyl et al. (2000a) should not be used to establish the validity of data, as it has been discounted by more recent and solid evidence. It is surprisingly that dose-related degeneration of the testicular germinal epithelium is questioned as adverse effect, as it is a pathologic alteration. It is long-time established knowledge that the rodent spermatogenesis has a much greater functional reserve than the human one, i.e., a 20% reduction in spermatogenesis has no impact on reproductive performance in rodents while it may have an impact in humans. Therefore, an appropriate NOAEL for male reproductive toxicity should consider the histopathology of testis (and accessory glands) and sperm parameters as potentially human-relevant endpoints, even in the absence of an appreciable decrease of male reproductive performance which might remain undetected in rodent standard studies. It is also questionable the relevance of the comment that this lesion was not observed in two old (Johnson et al., 1986; Friedman et al., 1995) and two recent (NTP, 2012, 2013) 2-year studies. Testicular lesions in such studies can easily be obscured by aging-related changes, whereas this does not occur in repeated-dose toxicity studies using young adult animals. Thus, the NOAEL for male reproductive toxicity could be reconsidered, with a strong focus on the studies performed after 2005 and assessing testicular histology and sperm parameters;
75	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	Lines 5270-87: It is not clear why, with several recent reproductive studies investigating the same dose range and showing effects, no attempt to calculate a BMD10 for male fertility effects is made. In the ensuing section 7.5.2. Dose-response assessment, lines 6906-7 it is stated that “The data on effects of AA on male reproduction were not suitable for dose-response modelling” however, no clear explanation is provided about why deriving a BMD10 is unfeasible. Since reproductive effects are identified as an important issue, this point could be discussed with more detail.
76	Istituto Superiore di Sanità (ISS)	Reproductive toxicity	Lines 5270-87: Additional comment: the Panel should consider to establish a NOAEL (or BMD10) for the endpoint "histopathological alterations of the male reproductive tissues"
77	Istituto Superiore di Sanità (ISS)	Developmental toxicity	Lines 5562-7. Additional comment: The Panel should consider to establish a NOAEL for the endpoint "persistent structural changes in the developing brain" (e.g., Ogawa et al., 2011); such NOAEL might be the basis to determine

			an overall NOAEL for developmental effects of acrylamide
78	Istituto Superiore di Sanità (ISS)	Developmental toxicity	General comment: As in the Reproductive Toxicity section I recommend to clearly separate the older studies (i.e., those performed before the JECFA assessment in 2005) from the more recent studies, which should be discussed and described in more detail.
79	Istituto Superiore di Sanità (ISS)	Developmental toxicity	Line 5326; please could you better explain “live pups per fetus” ?
80	Istituto Superiore di Sanità (ISS)	Developmental toxicity	Line 5491-5516: The current conclusions drawn on the study by Ogawa et al. (2012) are not clear: there is an irreversible structural change in a brain region and this is not considered adverse ? As it is expressed, this seems inconsistent with the rest of the draft opinion: AA is a recognized neurotoxicant and a potential developmental toxicants, so the overall evidence may allow to assess the biological relevance of early, but persistent, brain structural changes observed in one developmental study. Structural changes (if dose-related and properly characterized) can have a higher relevance for human health than “behavioral” changes, where the rodent-human exytrapolation can be really questionable. In the ensuing section 7.5.2. Dose-response assessment, lines 6900-1, it is concluded that “the most adequate endpoint for neurotoxicity was the incidence of peripheral nerve (sciatic) axonal degeneration observed in male F344 rats”, i.e., a structural effect is used to establish the current BMD10 for non-cancer endpoints. Therefore, the possible relevance of the study by Ogawa et al. in the definition of a developmental NOAEL could be reconsidered.
81	Istituto Superiore di Sanità (ISS)	Endocrine/reproductive toxicity	Line 5822: Should the title of this section be “Reproductive/developmental toxicity” ? Indeed, the section discusses possible endocrine-related (as well as non-endocrine) mechanisms of reproductive/developmental effects, which are among the main non-cancer endpoints identified by the draft opinion.

82	Istituto Superiore di Sanità (ISS)	Endocrine/reproductive toxicity	General comment: The overall section is difficult to follow: what is the rationale of the sequence by which studies are presented and discussed ? A more readily understandable sequence would help the reader to agree with the conclusion of the draft opinion.
83	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Observations in humans	(a) The focus is largely on the marginal impact of relatively small and imperfectly measured variations in dietary intake, with smoking (including the additional exposure to acrylamide that it entails) treated as a potential confounding variable. However, such marginal effects are not directly relevant to the assessment of exposure-response, especially if smoking contributes more than diet to internal dose. While presentation of results stratified by smoking is helpful in this regard, it would be valuable also to consider the human evidence on risks in relation to total exposure to acrylamide from all sources. The studies that have examined risk of cancer in relation to haemoglobin adducts do this. However, the adduct levels are not necessarily representative of long term exposure. (b) When evaluating the studies of occupational exposures, results should be set in the context of estimated internal doses as compared with those from dietary sources in the general population. It would be helpful to know whether they are likely to have been similar in magnitude or orders of magnitude higher. (c) Another consideration should be the risk of relevant health outcomes in relation to smoking – about which there will often be quite a lot of information. Tobacco smoke contains many other toxic substances as well as acrylamide, but it seems unlikely that its other constituents would importantly protect against adverse effects of acrylamide. Thus, if smoking has a major impact on personal exposures to acrylamide, and there is good evidence that a health outcome is not importantly related to smoking, then it is reasonable to suggest that outcome is probably not caused by acrylamide. Such consideration might be relevant, for example, to colon and thyroid cancer. (d) The review carefully presents information about stratification by smoking and results on non-smokers – it may help to state that conclusions would be similar if considering results in non-smokers or results from (the small number of studies) with information on adducts. (e) Similarly, when reviewing reproductive and developmental outcomes, background data on associations of relevant outcomes with smoking might provide an upper estimate of risk for effects from dietary exposures to acrylamide. (f) At several points in the section on human studies, there is reference to “subsequent quintiles”. “Subsequent” means occurring after in time, and is not the right word here. “Increasingly higher quintiles” would be better.

84	Anonymous	Observations in humans	References to my comment: – BfR - Bundesinstitut für Risikobewertung, 2003: Bedeutung der Studie von Mucci et al. für die Risikobewertung von Acrylamid in Lebensmitteln. Stellungnahme des BfR vom 25.02.2003 [Relevance of the study of Mucci et al. for the risk assessment on acrylamide in food. BfR statement, 02-25-2003]. In: http://www.bfr.bund.de/cd/3862?index=65&index_id=4185, accessed September 2014 – BfR - Bundesinstitut für Risikobewertung, 2003: Bedeutung der Arbeit von Pelucchi et al. für die Risikobewertung von Acrylamid in Lebensmitteln. Stellungnahme des BfR vom 08.07.2003 [Relevance of the study of Pelucchi et al. for the risk assessment on acrylamide in food. BfR statement, 07-08-2003]. In: http://www.bfr.bund.de/cd/3862?index=65&index_id=4185, accessed September 2014 – Hedelin, Maria/Klingt, Åsa/Chang, Ellen T./Bellocco, Rino/Johansson, Jan-Erik/Andersson, Swen-Olof/Heinonen, Satu-Maarit/Adlercreutz, Herman/Adami, Hans-Olov/Grönberg, Henrik & Augustsson Bälter, Katarina, 2006: Dietary Phytoestrogen, Serum Enterolactone and Risk of Prostate Cancer: The Cancer Prostate Sweden Study, Cancer Causes & Control, Vol. 17, Issue 2, 169-180. In: http://www.jstor.org/stable/29736446, accessed September 2014 – Mucci, Lorelei A./Dickmann, P. W./Steineck, G./Adami, Hans-Olov & Augustsson, K., 2003: Dietary acrylamide and cancer of the large bowel, kidney, and bladder: Absence of an association in a population-based study in Sweden. In: British Journal of Cancer, Vol. 88, Issue 1, 84-89 – Mucci, Lorelei A./Dickmann, Paul W./Steineck, Gunnar/Adami, Hans-Olov & Augustsson, Katarina, 2003: Reply: Dietary acrylamide and cancer risk: additional data on coffee. In: British Journal of Cancer, Vol. 89, Issue 4, 775-776 – Mucci, Lorelei A. & Adami, Hans-Olov, 2005: The Role of Epidemiology in Under-standing the Relationship between Dietary Acrylamide and Cancer Risk in Humans. In: Friedman, M. & Mottram, D. (Hrsg.): Chemistry and Safety of Acrylamide in Food. Advances in Experimental Medicine and Biology, Vol. 561. Heidelberg, New York: Springer, 39-48 – Naruszewicz, Marek/Daniewski, Marek/Nowicka, Grazyna & Kozlowska-Wojcie-chowska, Malgorzata, 2003: Trans-unsaturated fatty acids and acrylamide in food as potential atherosclerosis progression factors. Based on own studies. In: Acta Mirobiologica Polonica, Vol. 52, Supplement, 75-81 – Naruszewicz, Marek/Zapolska-Downar, Danuta/Kosmider, Anita/Nowicka, Grazyna/Koz¬lowska-Wojciechowska, Malgorzata/Vikström, Anna C. & Törnqvist, Margareta, 2009: Chronic intake of potato chips in

			humans increases the production of reactive oxygen radicals by leukocytes and increases plasma C-reactive protein: a pilot study. In: American Journal of Clinical Nutrition, Vol. 89, 773-777 – Pelucchi, Claudio/Franceschi, Silvia/Levi, Fabio/Trichopoulos, Dimitrios/Bosetti, Cris-tina/Negri, Eva & La Vecchia, Carlo, 2003: Fried Potatoes and Human Cancer. In: In-ternational Journal of Cancer, Vol. 105, Issue 4, 558-560 – VWA - Food and Consumer Product Safety Authority, 2003: White paper on acrylami-de - Presented to the EFSA Advisory Forum for consideration. Outcome of the acryl-ami¬de workshop held in Brussels on March 28, 2003. In: http://www.efsa.europa.eu/en/af030703/docs/af030703-ax8.pdf, accessed September 2014 – Wilson, Kathryn M./Bälter, Katarina/Adami, Hans-Olov/Grönberg, Henrik/Vikström, Anna C./Paulsson, Birgit/Törnqvist, Margareta & Mucci, Lorelei A., 2009: Acrylamide exposure measured by food frequency questionnaire and hemoglobin adduct levels and prostate cancer risk in the Cancer of the Prostate in Sweden Study. In: International Journal of Cancer, Vol. 124, Issue 10, 2384-2390
85	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Occupational studies and cancer	It was noted that EFSA had concluded that epidemiological studies of occupational exposure to acrylamide did not indicate an increased risk of cancer whereas earlier authors had judged that the evidence was suggestive of a risk (1). (1) Siemiatycki et al (2004) Environmental Health Perspectives 112 (15) pp 1447-1459. (2) The Burden of Occupational Cancer in the UK. Technical report: Pancreatic Cancer. Bagga et al.
86	Joint submission by the Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Dietary studies and cancer	The epidemiological studies are predominantly based on Food Frequency Questionnaire (FFQ) data. Such data are not very reliable, and the limitations should be explained better in the relevant discussion section, line 6621 onwards. In particular, a number of studies provided some validation information and this could be discussed further e.g. correlation coefficients comparing FFQ estimated intakes with those from food diaries and with measured adducts in Hb. In relation to the case-control studies, some discussion around possible biases should be included. Lines 6147-8 refer to assessment of habitual diet 20 years before interview by a validated food frequency questionnaire. A comment about the reliability of such data should be incorporated. The major limitation of the evidence above anything else is exposure misclassification and this should be mentioned

			at the start of the limitations (line 6608) due to limitations in estimation of both dietary and non-dietary exposure sources. Exposure misclassification is likely to have resulted in bias towards the null and it would be helpful to discuss if this is the key factor in why epidemiological studies in the general population have not found cancer risks (in contrast to animal studies), or whether this is a question of dose.
87	Anonymous	Dietary studies and cancer	We recommend to cite the recent literature review by Virk-Baker et al. 2014 in the section on Observations in humans, Epidemiological studies cancer in which the authors concluded that there is limited epidemiological evidence of associations between dietary acrylamide and various cancers and that the inadequate dietary assessment used in most studies hinders. Virk-Baker MK, Nagy TR, Barnes S, Groopman J. Dietary acrylamide and human cancer: a systematic review of literature. Nutr Cancer. 2014 Jul;66(5):774-90.
88	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Epidemiological studies: pre-natal exposure	It should be considered whether caffeine could have been the cause of the effects observed in the Norwegian Mother and Child Cohort.
89	Anonymous	Reproductive/developmental consequences	Please change the word *'showed'* with *'suggested'* in the text of the section on Epidemiological studies: pre-natal exposure, Reproductive/developmental consequences, p. 174, l. 6685. Please add the following to the section on Epidemiological studies: pre-natal exposure, Reproductive/developmental consequences, p. 174, l. 6694 after head circumference: "*as well as increased risk of being small for gestational age*." We suggest adding at p. 175, l. 6733 the following text: "*In the study which relied on Hb adducts (Pedersen et al. 2012) monotonic dose–response associations of AA exposure with birth outcomes were observed in women who were nonsmokers in pregnancy, as well as in never-smokers, even after adjusting for passive smoking based on self-reporting or using ethylene oxide Hb adducts as biomarkers of exposure to tobacco smoke. The associations between AA exposure and birth weight were consistent across the five countries*." We would like to inform you that a study, which is not yet published, but it is in preparation, with the French EDEN mother-child cohort have estimated maternal intake of AA using FFQ and that the authors have informed us that their findings are in line with those cited by Pedersen et al. 2012 and Duarte-Salles et al 2013. In this French study of 1,471 mother-child pairs, maternal intake of AA has been assessed by combining FFQ data on maternal dietary habits with data on AA concentration in foods provided by the second French total diet study. The estimated mean ± SD of maternal dietary exposure to acrylamide during pregnancy was 18.2 10.3 ± 14.2 103 ng/day. One SD increase in the estimated maternal dietary intake of AA was associated with an increased risk of small for gestational age (OR=1.20,

			95% CI: 1.04, 1.39) as well as reduced birth weight (-17 g (95% CI: -37, -3) (pers. comment M Kadawathagedara et al. 2014) – M Kadawathagedara, A Chan Hon Tong, B Heude, A Forhan, MA Charles, V Sirot and J Botton. Dietary acrylamide exposure during pregnancy and anthropometry at birth in the EDEN mother-child cohort study (pers. communication July 28, 2014).
90	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Epidemiological studies: neurological alterations	Data on exposures resulting in neurotoxicity, or discussion of why such exposures cannot be meaningfully characterised, would be helpful.
91	Joint submission by the Technical University of Denmark (DTU), the French Agency for Food, Environmental and Occupational Health & Safety (ANSES), and the Swedish National Food Agency (NFA Sweden)	Epidemiological studies	With reference to the recently released draft scientific opinion on acrylamide in food we would like to draw attention to a few important aspects of the risk assessment. First of all we are pleased to receive the first complete EFSA risk assessment of acrylamide. The opinion is very thorough and comprehensive. We are however concerned that the inconclusive nature of the epidemiological studies are somewhat interpreted to abate the otherwise clear results from the toxicological animals studies. As described by the EFSA opinion, acrylamide and its metabolite glycidamide are shown to be carcinogenic to rats and mice of both sexes. The reactive epoxide, glycidamide, has been shown to be genotoxic *in vitro* and *in vivo*. In humans as well as in rodents acrylamide is metabolised into glycidamide. Although we might not yet have the final scientific proof for acrylamide being a human carcinogen, it is most likely that acrylamide is carcinogenic in humans by the same mechanisms that causes cancer in rodents the calculated margin of exposure for neoplastic effects as calculated by EFSA, is in the range of 567-89 for the average consumer. This margin of exposure is very far from the 10.000 that would constitute a low concern (EFSA, 2012). We would suggest that the risk assessment clearly outlines the perspectives as per how unequivocal and clear results from animal toxicological studies should be interpreted in a situation where human epidemiological studies are equivocal. Furthermore, we would like to draw your attention to the reason why the human epidemiological studies are equivocal. In relation to the somewhat inconclusive situation around the epidemiological studies, we would have to maintain that this is by no means surprising. As shown in the attached, not-yet published article (Wielinga et al.). The statistical power of the hitherto conducted epidemiological studies are limited. It would be very difficult to detect the relatively low increase in cancer incidence as predicted from the animal experiments through studies with such low statistical power. In the epidemiological studies where a significant cancer effect was nevertheless found, the statistical power was most likely increased because of a more accurate estimation of the acrylamide exposure in the population investigated. In general, in cases where the epidemiological studies show clear positive (or negative)

			correlations they should weigh heavily in any risk assessment. As noted by Wielinga et al. the methodology used in the vast majority of epidemiological studies is often too insensitive to detected minor increases in cancer incidence, in particular when it is difficult to accurately determine the individual lifetime exposure of a particular substance, as in the case of acrylamide. Thus, we would suggest that the risk assessment clearly describes and outlines how the statistical power of human epidemiological studies can and should be included in the evaluation of the epidemiological evidence. It is important to note that studies with too low statistical power to detect the expected increase in cancer rate cannot show that such increase has not occurred. This advocates for caution in using the current epidemiological data to perform hazard identification and characterization. It is important to ensure that epidemiological data is not interpreted in a way that reduces the weight of evidence of animal data. With regard to the analysis of epidemiological studies, the report lists all cancers observed in epidemiological studies one after the other. While this approach has the advantage of systematically analysing lines of evidence in response to a specific issue, it can cause the corpus of data and publications to become over-fragmented, ultimately meaning that there is not sufficient perspective to judge a set of arguments that may be a part of a continuum of similar effects. Finally as the concept of margin of exposure is not well understood by people who are not toxicologist, it would assist the risk managers to use a more descriptive language to communicate the EFSA panels level of concern in their final risk characterization. References EFSA Journal 2012;10(3):2578. Scientific opinion. Statement on the applicability of the Margin of Exposure approach for the safety assessment of impurities which are both genotoxic and carcinogenic in substances added to food/feed. EFSA Scientific Committee. European Food Safety Authority (EFSA), Parma, Italy. Wielinga, Peter R., Elisabeth Wreford Andersen, Anja Olsen, Pelle Thonning Olesen, Henrik Lauritz Frandsen, Kit Granby, Bjarne Kjær Ersbøll & Jørgen Schlundt (to be submitted): A review of the effect of statistical design used in epidemiological studies of acrylamide intake relative to the predictive capacity of such studies in estimating human cancer risk. Article in preparation.
92	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Dose-response assessment	Is the proposed critical BMDL for neurological effects in rats likely to be lower than the exposures that have given rise to human neurotoxicity.

93	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Risk characterisation	The Risk Characterisation should be expanded to consider the context of other sources of exposure.
94	Chilean Food Quality and Safety Agency (ACHIPIA)	Risk characterisation	In general, the presentation of identification and characterization of risk is well focused, from the absorption form of AA, metabolization, neurotoxic and genotoxic effects to carcinogenicity, among others. On the other hand, the risks on human health are the same as those communicated for the very first time by Swedish researchers in April of 2002. That is, AA is a chemical genotoxic compound and potentially carcinogenic formed in food processing of common food products like potato chips, bread, biscuits, coffee, etc. Apparently there are no concluding results since studies are not perfectly standardized. Mitigation processes in the Tool-Box are useful for the industry. New procedures have been developed and the question here is how massive is the application of these recommendations by companies producing these foods, since with the exception of some baby foods, there are no significant reductions in the levels of AA in key foods.
95	Chilean Food Quality and Safety Agency (ACHIPIA)	Risk characterisation	The recommended values of 0.43 ppm for Neurotixic effects is equal to 430 ppb per kg, i.e. for an adult who weighs 70 kg, daily intake should be up to 30,100 ppb. In addition, recommended value of 0.17 ppm for Neoplastic effects equals to 170 ppb for an adult who weighs 70 kg and intake should be up to 11,900 ppb. The recommended values from 2013/647/EU commission are hence adequate since enable a daily intake of products under the risk limits (0,17 mg/kg). According to EFSA, the Margin of Exposure (MOE) is low for a genotoxic carcinogenic compound. However, studies to establish safety limits in food consumption must be improved according to the exposure level and type of food. European experts concluded that there is no risk of neurotoxicity from dietary intake of acrylamide. For infants, however, in 95 percentile MOE is very close to the limits regarding to neurotoxic effects. As concerns neoplasic effects, acrylamide is an “alarming” compound considering the uncertainty values and differences among species. Thus, there is a possible risk for permanent AA intake by different age groups worldwide, with no decrease in its content in food of regular consumption. Risk characterization developed by EFSA based on different studies, age groups and focused on neurotoxic and neoplasic effects should be analyzed. However, this applies to the consumption of a food group, not the total diet

			study, since the analyses are carried out in individual foods.
96	Anonymous	Uncertainty	Page 185, line 7096: suggesting that studies in which estimated dietary acrylamide intake (e.g., assessed with an FFQ) is correlated to AA Hb adducts are "validation studies" is overreaching. As suggested in e.g., Vikström et al., 2012, low correlations between the 2 exposure assessment methods is likely due to disadvantages of both methods. AA-Hb are prone to large intra-individual variation due to incidental intake of high-level acrylamide foods. In addition, AA-Hb are expressed per g of hemoglobin and hemoglobin levels vary intra and inter-individually due to extraneous factors, such as e.g., BMI, physical activity, heavy menstrual bleeding, alcohol intake, meat intake, etc. Page 185, lines 7096-7097: uncertainties in the measurement of AA intake in epidemiological studies may hamper reliably assessing its relation with cancer risk, but it is important to stress that this will only lead to underestimation of the strength of an association when one is found. Page 185, lines 7099-7100: it is questionable to state that the fact that the occupational epidemiological studies did not observe clear risks contributes to the uncertainty whether acrylamide is a human carcinogen. These occupational studies namely included nearly only men and were thus not able to show risks in women (e.g., endometrial cancer), if any. Studies in rats/mice are also performed in both sexes for a reason, I would say. Considering the fact that multiple dietary epidemiological studies of good quality showed associations with cancer risk (mainly endometrial, ovarian cancer) and that the 2 studies on developmental toxicity (birth outcomes) performed so far showed clear reductions in prenatal growth, the impact of the uncertainties on the risk assessment of human exposure to AA through consumption of food is not moderate, but major. The risks of cancer in the epidemiological studies are namely much higher than calculated based on the rodent data (based on the rodent calculations, risks would be so low that they could never have been picked up in epidemiological studies, yet they were in some studies). In addition, if the epidemiological associations between dietary acrylamide intake and birth outcomes are true, then there is no MOE for developmental exposure at all. Can EFSA with absolute certainty exclude the possibility that humans are more sensitive to acrylamide than rodents? The mentioned uncertainties (on pages 183-186) are miniscule compared to the uncertainty that is introduced by disregarding the epidemiological findings in the way that is done in this opinion. The studies on cancer may be limited and inconsistent and it may not be clear if the association between dietary AA exposure and birth outcomes is causal, but that does not mean that the findings can be ignored in the risk assessment and certainly not in the assessment of the uncertainties associated with the risk assessment done. Another study on dietary acrylamide and endometrial cancer risk was recently published: Obón-Santacana M et al. Dietary intake of acrylamide and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition cohort. Br J Cancer. 2014 Aug 26;111(5):987-97. It again showed increased risk, in never-smokers and

			never-users of oral contraceptives, a subgroup that is quite similar to the NLCS never-smoking population in which an increased risk was observed too.
97	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Uncertainty	It would be useful to summarise the most important sources of uncertainty.
98	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Summary of uncertainties	It is unclear why the entry relating to occupational studies in Table 31 indicates underestimation of exposure/risk
99	Anonymous	Conclusions and recommendations	Page 192, recommendations: - Is EFSA not of the opinion that more epidemiological studies on dietary acrylamide intake and cancer risk are needed? - What is the opinion of EFSA on epidemiological studies on dietary acrylamide intake and neurotoxicity? Richard LoPachin has repeatedly suggested in his papers that studies in this field are indicated. Considering the fact that studies in workers have shown effects on the central nervous system and the fact that these effects may not be reversible and are thus cumulative over time suggests that chronic high dietary acrylamide intake may be able to contribute to neurological diseases such as Alzheimer's and Parkinson's disease. In addition, acrylamide could perhaps also lead to impaired cognitive development.
100	Istituto Superiore di Sanità (ISS)	Conclusions and recommendations	Line 7369 and followings. Further recommendations could include: - adequate data on the AA effects on reproductive development and maturation (from organogenesis to puberty) - clarification on the relevance of possible endocrine-related mechanisms for reproductive and developmental effects as well as for tumour development in specific target tissues in rodents and humans - clarification on developmental neurotoxicity mechanisms and on the link between early molecular/structural changes and possible adverse outcomes in later life.

			More data on the above issues would support AA risk assessment for potentially vulnerable lifestages, like infants, toddlers and children (see also Table 29).
101	FoodDrinkEurope (FDE)	Conclusions and recommendations	Occurrence Lines 7171-7172: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only. The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): • Roasted coffee (dry): 249 • Instant coffee (dry): 710 • Substitute coffee (dry), based on cereals: 510 • Substitute coffee (dry) based on chicory: 2942 • Substitute coffee (dry) unspecified: 415 It has to be noted that the markets for coffee and for coffee substitutes are hugely different in volume. Based on Eurostat/Prodcom data we calculate that the size of the coffee substitutes market is 2,3% of that of the coffee market. The statement that AA was found at the highest levels in 'Coffee and coffee substitutes' gives the impression that this is the case across all sub-categories, while in fact it is correct only for the much smaller market of the chicory-based

			coffee substitutes. We therefore propose: • To split the 'coffee and coffee substitutes' into the two sub-categories. • To refer to acrylamide levels in coffee and in coffee substitutes as consumed The statement that AA was found at the highest level in 'coffee and coffee substitutes' should be revised accordingly. Line 1786: It is stated that 'roasted coffee' was found to be less contaminated than 'instant coffee' on basis of the analysis of the 'dry (as sold)' products. This is less relevant than the comparison of the levels in the products 'as prepared for consumption'. When taking the averages (mean middle bound values: Roast coffee: 249 µg/kg; Instant coffee: 710 µg/kg) and the dilution factors 'Roast coffee: 0.053; Instant Coffee: 0.017) the mean level for 'as prepared for consumption' for roast coffee is 13.2 µg/l respectively 12.1 µg/l for instant coffee. This leads to the conclusion that levels of acrylamide in both sub-categories are at a similar/ not significantly different level.
102	National Coffee Association USA (NCA)	Conclusions and recommendations	1. Abstract, line 7171-7172: The statement that, "*AA was found at the highest levels in 'Coffee and coffee substitutes', followed by 'Potato crisps and snacks' and 'Potato fried products'*" may be technically correct. However, it is very misleading because the levels in coffee and coffee substitutes are based on the dry product whereas the levels for potato crisps and snacks and potato fried products are based on the products as prepared for consumption. An "apples-to-apples" comparison of AA levels in coffee and coffee substitutes as consumed to AA levels in other consumed foods would show that many other food categories contain higher AA levels relative to coffee and coffee substitutes. We recommend that all comparisons of AA levels in different food categories be made in terms of food or beverage "as consumed" and that the statement "AA was found at the highest levels in 'Coffee and coffee substitutes'," be revised accordingly.
103	National Coffee Association USA (NCA)	Conclusions and recommendations	2. Conclusions and recommendations, line 7171-7172: The food category "coffee and coffee substitutes" is comprised of several subcategories with very different AA levels in the dry product. As shown in Table 6 (line 1359), the mean value for "roasted coffee (dry)" is 249 micrograms per kilogram (µg/kg), as compared to mean values of 710 µg/kg for "instant coffee (dry)," 510 µg/kg for "substitute coffee (dry), based on cereals," 2,942 µg/kg for "substitute coffee (dry), based on chicory," and 415 µg/kg for "substitute coffee (dry), unspecified." These data clearly indicate that AA levels differ between these categories, particularly substitute coffee based on chicory. We recommend that "coffee" and "substitute coffee" be treated as separate food categories.

104	Renaissance BioScience Corp.	Conclusions and recommendations	Lines 7142 – 7146: Conclusions and recommendations. Renaissance BioScience's (www.renaissancebioscience.com) acrylamide-preventing baker's yeast has been shown in extensive testing with many commercial partners to reduce the presence of acrylamide in the spectrum of affected food products ranging from baked products, potato-based foods, to coffee and others. This acrylamide-preventing yeast (AP yeast) – which, aside from an accelerated ability to consume asparagine, is identical to parental Saccharomyces cerevisiae (baker's yeast) in every other way – is classically developed and non-GMO and is expected to be available for commercial sales beginning in 2015. Its ease of use makes it ideal for any size food manufacturer or processor ranging down to the home kitchen, and will make it an invaluable addition to the AA reducing toolbox as a fast-emerging, natural acrylamide-preventing food processing technology that food manufacturers will find efficient and reliable. This novel emerging technology should be actively considered for inclusion in the Acrylamide Toolbox.
105	Renaissance BioScience Corp.	Conclusions and recommendations	Lines 7179 – 7181: Conculsions and recommendations Renaissance BioScience's (www.renaissancebioscience.com) acrylamide-preventing baker's yeast has been shown in extensive testing with commercial partners to reduce the presence of acrylamide in yeast-fermented baking products. This will eliminate the acrylamide threat in baked bread and the elevated AA presence that occurs when bread or buns are toasted in the home or restaurant. This acrylamide-preventing yeast (AP yeast) – which, aside from an accelerated ability to consume asparagine, is identical to parental *Saccharomyces cerevisiae* (baker's yeast) in every other way – is classically developed and non-GMO and is expected to be available for commercial sales beginning in 2015.
106	Joint submission by the UK Committee on Toxicity (COT) and UK Committee on Carcinogenicity (COC)	Conclusions and recommendations	Given the effects on the rodent testis, a comment on the possibility of transgenerational effects, would be useful together with a recommendation for research. In relation to the third recommendation, it was noted that urinary metabolites would be unlikely to show a direct correlation to dietary exposure because of the importance of other sources of exposure.
107	Anonymous	Conclusions and recommendations	Since 2010 a BMDL10 of 0.16-0.18 mg has been calculated by the international agencies instead of 0.3 mg in the time before. This means that in experimental animals acrylamide is more effective than previously assumed. The carcinogenicity of acrylamide is def-initely better proven than before – a confirmation of IARC's 1994 risk assessment. IARC (2006) explained that all substances which have been identified so far as being carcinogenic to

			humans are carcinogenic to animals as well. One cannot conclude that each substance which causes cancer in animals must have the same effect to humans. However, according to IARC, this assumption is plausible as long as the relation has been proven sufficiently in experimental animal studies. According to the basic princi-ples of consumer protection, regulatory measures are justified in situations as this (EC 2000) – i.e. when there is no certainty but a well-founded suspicion about the carcino-genicity of a substance. Conclusion: => Moderate benefits for the consumers: The carcinogenicity of Acrylamide in experimental animals is better proven than before. One can conclude now that the substance is "very probably carcinogenic" to humans. Risk management actions would have been justified already on the basis of the 1994 risk assessment. Hence measures to reduce the exposure are strongly indicated. (Please read my comment as a whole. I sent it via E-Mail) References: – EC - European Commission, 2000: Communication from the Commission on the pre-cautionary principle. COM/2000/0001 final. In: http://eur-lex.europa.eu/legal-content/DE/ALL/;ELX_SESSIONID=rhCwJN4JNMfdvGfky4hd1ppYmBL6zkX9GdBZBC0kpyvZnkTBv6hH!2122051397?uri=CELEX:52000DC0001, accessed September 2014 – IARC - International Agency for Research on Cancer, 1994: Acrylamide. IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, 60. Lyon, France: IARC. In: http://monographs.iarc.fr/ENG/Monographs/vol60/index.php, accessed September 2014 – IARC - International Agency for Research on Cancer, 2006: Preamble to the IARC Monographs (amended January 2006). Lyon, France: IARC. In: http://monographs.iarc.fr/ENG/Preamble/index.php, accessed September 2014
108	Anonymous	Conclusions and recommendations	In 2005, Jecfa recommended to reduce the acrylamide Levels (WHO, 2006). In the following assessments the MOE remained low and acrylamide was again called a "concern", but no recommendations were given. Instead it did follow huge lists of research wishes. It is obvious that just more research is not in the consumers' best interest. After the 2014 risk assessment many questions remain open: How useful is a risk assessment without any recommendations? The risk manager is usually not an expert in epidemiology, exposure assessment and toxicology. Did DG Sanco ask for a new risk assessment without wishing a recommendation from the scientists, judging their

			findings and contemplating the options to reduce the risk? What does it mean if acrylamide is called a "concern", but no consequences follow? Does EFSA really not recommend any risk management action facing a MOE which is below 500? The BfR developed guidelines for risk assessments which provide a recommendation in every case. Consequently, it has to be mentioned explicitly when no action is recommended (BfR, 2010). Why was the concept of MOE introduced if even at a low MOE no recommendation is given? How low must the MOE be before any recommendation will be given? A risk assessment without any recommendation is not convincing. The concept of MOE sounds plausible but it does not make sense if no recommendation follows when the MOE is as low as it is for acrylamide. Thus, the recommendation can only be reduction of the exposure – accompanied by a systematic monitoring which makes trends visible. If EFSA will not recommend the reduction, it does not act according to the principles of the MOE. In no case does the society need to spend more resources on the research on acrylamide. (Please read my comment as a whole. I sent it via E-Mail) Reference: – BfR - Bundesinstitut für Risikobewertung, 2010: Leitfaden für gesundheitliche Bewer-tungen. Ausgabe 2010 [Guideline for risk assessments. Edition 2010]. In: http://www.bfr.bund.de/cm/350/leitfaden-fuer-gesundheitliche-bewertungen.pdf, accessed Septem-ber 2014 – WHO - Word Health Organization, 2006: Evaluation of Certain Food Contaminants. Sixty-fourth report of the Joint FAO/WHO Expert Committee on Food Additives. WHO Technical Report Series No. 930, 2006. In: http://www.who.int/foodsafety/publications/jecfa-reports/en/, accessed September 2014
109	European Coffee Federation (ECF)	Conclusions and recommendations	Line 7171-7172: It is stated that AA was found at the highest levels in 'Coffee and coffee substitutes'. a) Comparison on 'as prepared for consumption' only. The statement refers to acrylamide levels in 'dry (as sold)' coffee and coffee substitute products which are not consumed as such. This may technically be correct but is seen not relevant by the European Coffee Federation in a context of an exposure assessment and risk assessment. It may even be misleading when comparing these levels with other products which are consumed as sold. It is acknowledged that in the assessment conversion factors are being applied to result in levels as prepared for consumption, which should be the only basis for any comparison. We accordingly propose to avoid a comparison on a semi-finished product basis and to only compare categories/sub-categories on the basis of levels as consumed respectively on the basis of their relative contribution to the total

			exposure to acrylamide. b) Assessment on relevant sub-category basis only. The grouping together of coffee and coffee substitutes in a single category is seen as inappropriate by the European Coffee Federation as these are independent sub-categories which need to be assessed separately. According to Table 6 (lines 1359-1360) the mean middle bound levels found in the sub-categories of this category are (µg/kg): - Roasted coffee (dry): 249 - Instant coffee (dry): 710 - Substitute coffee (dry), based on cereals: 510 - Substitute coffee (dry) based on chicory: 2942 - Substitute coffee (dry) unspecified: 415 It has to be noted that the markets for coffee and for coffee substitutes are hugely different in volume. Based on Eurostat/Prodcom data we calculate that the size of the coffee substitutes market is 2,3% of that of the coffee market. The statement that AA was found at the highest levels in 'Coffee and coffee substitutes' gives the impression that this is the case across all sub-categories, while in fact it is correct only for the much smaller market of the chicory-based coffee substitutes. We therefore propose: - To split the 'coffee and coffee substitutes' into the two sub-categories. - To refer to acrylamide levels in coffee and in coffee substitutes as consumed The statement that AA was found at the highest level in 'coffee and coffee substitutes' should be revised accordingly.
110	European Coffee Federation (ECF)	Conclusions and recommendations	Line 7186: It is stated that 'roasted coffee' was found to be less contaminated than 'instant coffee' on basis of the analysis of the 'dry (as sold)' products. This is less relevant than the comparison of the levels in the products 'as prepared for consumption'. When taking the averages (mean middle bound values: Roast coffee: 249 µg/kg; Instant coffee: 710 µg/kg) and the dilution factors 'Roast coffee: 0.053; Instant Coffee: 0.017) the mean level for 'as prepared for consumption' for roast coffee is 13.2 µg/l respectively 12.1 µg/l for instant coffee. This leads to the conclusion that levels of acrylamide in both sub-categories are at a similar/ not significantly different level.

111	Chilean Food Quality and Safety Agency (ACHIPIA)	Conclusions and recommendations	The conclusions and recommendations of the document from EFSA are apparently very accurate regarding the AA content in food and its potential risk for human health. The results indicate the real presence of AA in some foods. Therefore, from the revision of the document from EFSA, the Panel of Experts on Acrylamide coordinated by ACHIPIA in Chile analyzes the following points: - The main problem lies in the disparity of results in food consumption among different European countries, for example in starchy food whose consumption is specific in certain countries. In addition, it is important to consider the source of raw materials used in the elaboration and preparation of products. It is recommended to continue the research, considering this report from EFSA. - At a technical level, the effect of the heat load of different industry processes on AA formation must be studied. It is recommended to evaluate the effect of microstructure on the AA formation in food and its bio-availability and bio-accessibility. At the same time, since there are no concluding studies related to mutagenic effects, it is suggested further investigation to go into detail in this regard. Since there are no significant changes in most of the assessed food categories, the reliability of trend analysis and risk assessment is limited. - It is recommended to continue the research on mitigation processes so as to reduce the AA content in fried, baked, high consumption extruded food, as well as agronomic research for the development of new varieties of low asparagine potatoes, biologic markers control of AA intake in different age groups and urinary metabolites, etc. - Likewise, it is considered to continue the revision of research work worldwide, in which relevant subjects are studied such as AA formation and degradation kinetics, mechanisms for its reduction, instrumental methods for its determination and experimental results from both experimental models and usual processing of different foods. - The preparation of samples (high-temperature processing) before the analysis is emphasized. This point is fundamental since insignificant differences in processing can considerably affect the results. - Regarding analytical methods, it is important to associate studies of consumption intake in a given adult population with the determination of biologic biomarkers like AA-HB adducts, Glycidamide-HB and renal excretion metabolites. In this regard, further studies on biomarkers should be carried out in order to validate its application and reference methodology, as a solution for possible deviations caused by error in surveys. On the other hand, the scientific community points out the need for developing analytical methodologies based on more reachable that can be used in the routine control in food products. - In regard to the risk communication, an assessment in the dissemination of this subject at consumers' level is considered to reduce acrylamide in handling, preparation and elaboration of food. Workshops are recommended for professionals from processing industries of food with higher levels of AA, informing and disseminating mitigation

			procedures (Tool Box) and including the new procedures in literature. -The level of exposure must be on scale-level, so as to make the interpretation of results easier according to the variability of products, preparation and consumption habits. - The diversity of raw materials for different foods, the kind of process and the type of matrix of food directly related to its chemical composition must be considered. Consequently, the type of extraction of AA must be specified according to the matrix and processing.
112	Chilean Food Quality and Safety Agency (ACHIPIA)	Conclusions and recommendations	It is important to analyze the AA intake from the point of view of total diet, not a group of critical foods, since AA intake can be overestimated. Therefore, if the intake is estimated with this methodology, it should be expressed according to extreme consumers, since if we consider it as a typical diet, AA concentration could be insignificant. Regarding procedures and/or regulations, the FoodDrinkEurope has some guidelines to reduce acrylamide in the elaboration of diverse groups of food and Codex Code of Practice's task is to advice the authorities and manufacturers to prevent and reduce acrylamide in potato and cereals based products. This perspective includes three strategic lines: raw materials, control/addition of other ingredients and elaboration and heat treatment of foods. It is also important to keep intact nutritional qualities, as well as organoleptic characteristics and consumer's acceptation. It means that all reduction strategies must be assessed depending on their benefits and possible adverse effects. Notwithstanding, the public consultation document from EFSA raises some reservations: It is interesting that Joint FAO/WHO Expert Committee on Food Additives (JECFA) could establish concentrations with No Observed Adverse Effect Level (NOAEL) for neurologic effects and other non-neoplastic effects when reviewing the new information available. Acrylamide in breast milk is noteworthy. It is recommended, therefore, further investigation.
113	Anonymous	Documentation provided to EFSA	Some papers are not included in this draft opinion: – Clement et al. Expression profile of human cells in culture exposed to glycidamide, a reactive metabolite of the heat-induced food carcinogen acrylamide.Toxicology. 2007 Oct 30;240(1-2):111-24. – Mannaa F1, Abdel-Wahhab MA, Ahmed HH, Park MH. Protective role of Panax ginseng extract standardized

			with ginsenoside Rg3 against acrylamide-induced neurotoxicity in rats. J Appl Toxicol. 2006 May-Jun;26(3):198-206. – Naruszewicz M, Zapolska-Downar D, Kośmider A, Nowicka G, Kozłowska-Wojciechowska M, Vikström AS, Törnqvist M. Chronic intake of potato chips in humans increases the production of reactive oxygen radicals by leukocytes and increases plasma C-reactive protein: a pilot study. Am J Clin Nutr. 2009 Mar;89(3):773-7. In the paper of Hochstenbach et al. 2012, it is reported that correlations between AA-Hb and micronuclei and GA-HB and micronuclei in cord blood of 45 male newborns were 0.75 and 0.73, respectively. This is not reported on in the EFSA opinion.
114	Novozymes A/S	References	References pertaining to our input to section 4.4.2 "Impact on processing": – Hendriksen HV, Kornbrust BA, Oestergaard PR and Stringer MA, 2009. Evaluating the potential for enzymatic acrylamide mitigation in a range of food products using an asparaginase from Aspergillus oryzae. J. Agric. Food. Chem, 57, 4168-4176. – Hendriksen HV, Budolfsen G and Baumann MJ, 2013. Asparaginase for acrylamide mitigation in food, in Acrylamide, furans and other food-borne contaminants, from plant science to food chemistry. Aspects of Applied Biology, 116. – Kornbrust BA, Stringer MA, Lange NEK and Hendriksen HV, 2010. Asparaginase – an enzyme for acrylamide reduction in food products. In Enzymes in Food Technology, 2nd. Edition, pp. 59-87. Eds. R Whitehurst and M van Oort. Wiley-Blackwell. – FoodDrinkEurope Acrylamide Toolbox 13th update
115	European Coffee Federation (ECF)	Appendices	Line 9334-9335: The term ‘coffee Americano’ is not a common term across Europe. We would propose to replace it with ‘drip filter coffee’.
116	European Coffee Federation (ECF)	Appendices	Line 9350: The term ‘café américano’ is not a common term across Europe. We would propose to replace it with ‘drip filter coffee’.
117	European Coffee Federation (ECF)	Appendices	Line 9350: It would be interesting to have more details on the data for ‘Unspecified coffee (Beverage)’ since this

			covers a significant number of samples. We understand that the EFSA Evidence Management Unit is working on a few database corrections, updates and detailed data, and that the CONTAM Panel will take these into consideration in finalising the draft opinion after the consultation period. We very much welcome and appreciate this.
118	European Coffee Federation (ECF)	Appendices	Line 9353: The dilution factor used to recalculate from coffee substitutes (solids) to coffee substitutes (beverage) is 0.125. This is not in accordance with actual market practice and advices for product preparation. The dilution factor should be 0.02. (More specifically, the dilution factor of 0.02 only applies to 'as sold' soluble coffee substitute products and a different factor in the same magnitude as the dilution factor for drip filter coffee should be taken for 'as sold' roast & ground coffee substitute products).
119	European Coffee Federation (ECF)	Appendices	Line 9390: The term 'café américano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'.
120	FoodDrinkEurope (FDE)	Appendices	Note under table C3. Lines 9334-9335: The term 'coffee Americano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'. Table D1. Line 9350: The term 'café américano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'. It would be interesting to have more details on the data for 'Unspecified coffee (Beverage)' since this covers a significant number of samples. We understand that the EFSA Evidence Management Unit is working on a few database corrections, updates and detailed data, and that the CONTAM Panel will take these into consideration in finalising the draft opinion after the consultation period. We very much welcome and appreciate this. Line 9353: The dilution factor used to recalculate from coffee substitutes (solids) to coffee substitutes (beverage) is 0.125. This is not in accordance with actual market practice and advices for product preparation. The dilution factor should be 0.02. (More specifically, the dilution factor of 0.02 only applies to 'as sold' soluble coffee substitute products and a different factor in the same magnitude as the dilution factor for drip filter coffee should be taken for 'as sold' roast & ground coffee substitute products). Table D8. Line 9390: The term 'café américano' is not a common term across Europe. We would propose to replace it with 'drip filter coffee'.

Appendix B. List of studies considered in the risk assessment after endorsement of the draft opinion for public consultation

The literature search carried out to inform the draft opinion on acrylamide (AA) in food endorsed for public consultation by the CONTAM Panel on 15 May 2014 covered until 5 May 2014. Since the endorsement of the draft opinion, additional studies have been published in the open literature in relation to the hazard identification and characterisation of AA. These studies were identified and selected following the same approach as described in Appendix A of the draft opinion. The search was performed to cover until 13 March 2015.

The result of the study selection process identified 51 additional studies published in the open literature related to the hazard identification and characterisation of AA since the cut-off date of the endorsed draft opinion. The selection of the studies for inclusion or non-inclusion in the hazard characterisation was the same as for the draft Scientific Opinion.

The additional studies included in the opinion (EFSA CONTAM Panel, 2015) since endorsement are listed below (in alphabetical order according to the first author):

1. Ali MA, Aly EM and Elawady AI, 2014. Effectiveness of selenium on acrylamide toxicity to retina. International Journal of Ophthalmology, 7, 614–620.

2. Chen W, Shen Y, Su H and Zheng X, 2014. Hispidin derived from *Phellinus linteus* affords protection against acrylamide-induced oxidative stress in Caco-2 cells. Chemico-Biological Interactions, 219, 83–89.

3. Chiang WC, Chen CY, Lee TC, Lee HL and Lin YW, 2015. Fast and simple screening for the simultaneous analysis of seven metabolites derived from five volatile organic compounds in human urine using on-line solid-phase extraction coupled with liquid chromatography-tandem mass spectrometry. Talanta, 132, 469–478.

4. Fang J, Liang CL, Jia XD and Li N, 2014. Immunotoxicity of acrylamide in female BALB/c mice. Biomedical and Environmental Sciences, 27, 401–409.

5. Huang CC, Wu CF, Shih WC, Luo YS, Chen MF, Li CM, Liou SH, Chung WS, Chiang SY and Wu KY, 2015a. Potential association of urinary N7-(2-Carbamoyl-2-hydroxyethyl) guanine with dietary acrylamide intake of smokers and nonsmokers. Chemical Research in Toxicology, 28, 43–50.

6. Huang YS, Hsieh TJ and Lu CY, 2015b. Simple analytical strategy for MALDI-TOF-MS and nanoUPLC-MS/MS: quantitating curcumin in food condiments and dietary supplements and screening of acrylamide-induced ROS protein indicators reduced by curcumin. Food Chemistry, 174, 571–576.

7. Ishii Y, Matsushita K, Kuroda K, Yokoo Y, Kijima A, Takasu S, Kodama Y, Nishikawa A and Umemura T, 2015. Acrylamide induces specific DNA adduct formation and gene mutations in a carcinogenic target site, the mouse lung. Mutagenesis, 30, 227–235.

8. Je Y, 2015. Dietary acrylamide intake and risk of endometrial cancer in prospective cohort studies. Archives of Gynecology and Obstetrics, 291, 1395–1401.

9. Kim K-H, Park B, Rhee D-K and Pyo S, 2015. Acrylamide induces senescence in macrophages through a process involving ATF3, ROS, p38/JNK, and a telomerase-independent pathway. Chemical Research in Toxicology, 28, 71–86.

10. Kim TH, Shin S, Kim KB, Seo WS, Shin JC, Choi JH, Weon KY, Joo SH, Jeong SW and Shin BS, 2015. Determination of acrylamide and glycidamide in various biological matrices by liquid chromatography-tandem mass spectrometry and its application to a pharmacokinetic study. Talanta, 131, 46–54.

11. Kotova N, Frostne C, Abramsson-Zetterberg L, Tareke E, Bergman R, Haghdoost S, Paulsson B, Tornqvist M, Segerback D, Jenssen D and Grawe J, in press. Differences in micronucleus frequency and acrylamide adduct levels with hemoglobin between vegetarians and non-vegetarians. European Journal of Nutrition, DOI 10.1007/s00394-014-0796-7.

12. Lebda M, Gad S and Gaafar H, 2014. Effects of lipoic Acid on acrylamide induced testicular damage. Materia Socio-Medica, 26, 208-212.

13. Lee JH, Lee KJ, Ahn R and Kang HS, 2014. Urinary concentrations of acrylamide (AA) and N-acetyl-S-(2-carbamoylethyl)-cysteine (AAMA) and associations with demographic factors in the South Korean population. International Journal of Hygiene and Environmental Health, 217, 751–757.

14. Lin CY, Lin LY, Chen YC, Wen LL, Chien KL, Sung FC, Chen PC and Su TC, 2015. Association between measurements of thyroid function and the acrylamide metabolite N-Acetyl-S-(propionamide)-cysteine in adolescents and young adults. Environmental Research, 136, 246–252.

15. Manjanatha MG, Guo LW, Shelton SD and Doerge DR, in press. Acrylamide-induced carcinogenicity in mouse lung involves mutagenicity: cII gene mutations in the lung of big blue mice exposed to acrylamide and glycidamide for up to 4 weeks. Environmental and Molecular Mutagenesis, DOI: 10.1002/em.21939.

16. Maronpot RR, Thoolen RJ and Hansen B, 2015. Two-year carcinogenicity study of acrylamide in Wistar Han rats with *in utero* exposure. Experimental and Toxicologic Pathology, 67, 189–195.

17. Mehri S, Shahi M, Razavi BM, Hassani FV and Hosseinzadeh H, 2014a. Neuroprotective effect of thymoquinone in acrylamide-induced neurotoxicity in Wistar rats. Iranian Journal of Basic Medical Sciences, 17, 1007–1011.

18. Mehri S, Meshki MA and Hosseinzadeh H, 2015. Linalool as a neuroprotective agent against acrylamide-induced neurotoxicity in Wistar rats. Drug and Chemical Toxicology, 21, 1–5.

19. Muralidhara PSN, 2014. Mitigation of acrylamide-induced behavioral deficits, oxidative impairments and neurotoxicity by oral supplements of geraniol (a monoterpene) in a rat model. Chemico-Biologial Interactions, 6, 27–37.

20. Nagata C, Konishi K, Tamura T, Wada K, Tsuji M, Hayashi M, Takeda N and Yasuda K, 2015. Associations of acrylamide intake with circulating levels of sex hormones and prolactin in premenopausal Japanese women. Cancer Epidemiology Biomarkers and Prevention, 24, 249–254.

21. Obón-Santacana M, Kaaks R, Slimani N, Lujan-Barroso L, Freisling H, Ferrari P, Dossus L, Chabbert-Buffet N, Baglietto L, Fortner RT, Boeing H, Tjonneland A, Olsen A, Overvad K, Menendez V, Molina-Montes E, Larranaga N, Chirlaque MD, Ardanaz E, Khaw KT, Wareham N, Travis RC, Lu Y, Merritt MA, Trichopoulou A, Benetou V, Trichopoulos D, Saieva C, Sieri S, Tumino R, Sacerdote C, Galasso R, Bueno-de-Mesquita HB, Wirfalt E, Ericson U, Idahl A, Ohlson N, Skeie G, Gram IT, Weiderpass E, Onland-Moret NC, Riboli E and Duell EJ, 2014. Dietary intake of acrylamide and endometrial cancer risk in the European Prospective Investigation into Cancer and Nutrition cohort. British Journal of Cancer, 111, 987–997.

22. Obón-Santacana M, Peeters PH, Freisling H, Dossus L, Clavel-Chapelon F, Baglietto L, Schock H, Fortner RT, Boeing H, Tjonneland A, Olsen A, Overvad K, Menéndez V, Sanchez MJ, Larranaga N, Huerta Castaño JM, Barricarte A, Khaw KT, Wareham N, Travis RC, Merritt MA, Trichopoulou A, Trichopoulos D, Orfanos P, Masala G, Sieri S, Tumino R, Vineis P, Mattiello A, Bueno-de-Mesquita HB, Onland-Moret NC, Wirfalt E, Stocks T, Idahl A, Lundin E, Skeie G, Gram IT, Weiderpass E, Riboli E and Duell EJ, 2015. Dietary intake of acrylamide and epithelial ovarian cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. Cancer Epidemiology, Biomarkers and Prevention, 24, 291–297.

23. Ozturan Ozer E, Ucar G, Helvacioglu F, Akaydin-Aldemir D and Turkoglu S, 2014. Effect of acrylamide treatment on arginase activities and nitric oxide levels in rat liver and kidney. Acta Medica Mediterranea, 30, 375–382.

24. Pelucchi C, Bosetti C, Galeone C and La Vecchia C, 2015. Dietary acrylamide and cancer risk: An updated meta-analysis. International Journal of Cancer, 136, 2912–2922.

25. Pourentezari M, Talebi A, Abbasi A, Khalili MA, Mangoli E and Anvari M, 2014. Effects of acrylamide on sperm parameters, chromatin quality, and the level of blood testosterone in mice. Iran Journal of Reproductive Medicine, 12, 335–342.

26. Raju J, Roberts J, Taylor M, Patry D, Chomyshyn E, Caldwell D, Cooke G and Mehta R, 2015. Toxicological effects of short-term dietary acrylamide exposure in male F344 rats. Environmental Toxicology and Pharmacology, 39, 85–92.

27. Ruenz M, Bakuradze T, Eisenbrand G and Richling E, in press. Monitoring urinary mercapturic acids as biomarkers of human dietary exposure to acrylamide in combination with acrylamide uptake assessment based on duplicate diets. Archives of Toxicology, DOI 10.1007/s00204-015-1494-9.

28. Sen E, Tunali Y and Erkan M, 2015. Testicular development of male mice offsprings exposed to acrylamide and alcohol during the gestation and lactation period. Human and Experimental Toxicology, 34, 401–414.

29. Song L, Wang J, Zhang W, Yan R, Hu X, Chen S and Zhao S, 2014. Effective suppression of acrylamide neurotoxicity by lithium in mouse. Neurochemical Research, 39, 2170–2179.

30. Syberg K, Binderup ML, Cedergreen N and Rank J, 2015. Mixture genotoxicity of 2,4-dichlorophenoxyacetic Acid, acrylamide, and maleic hydrazide on human caco-2 cells assessed with comet assay. Journal of Toxicology and Environmental Health A, 78, 369–380.

31. Virk-Baker MK, Nagy TR, Barnes S and Groopman J, 2014. Dietary Acrylamide and Human Cancer: A Systematic Review of Literature. Nutrition and Cancer, 29, 1–17.

32. Walters B, Hariharan V and Huang H, 2014. Dietary levels of acrylamide affects rat cardiomyocyte properties. Food and Chemical Toxicology, 71, 68–73

33. Wang ET, Chen DY, Liu HY, Yan HY and Yuan Y, 2015. Protective effect of allicin against glycidamide-induced toxicity in male and female mice. General Physiology and Biophysics, 34, 177–187.

34. Wei Q, Li J, Li X, Zhang L and Shi F, 2014. Reproductive toxicity in acrylamide-treated female mice. Reproductive Toxicology, 46, 121–128.

35. Yao X, Yan L, Yao L, Guan W, Zeng F, Cao F and Zhang Y, 2014. Acrylamide exposure impairs blood-cerebrospinal fluid barrier function. Neural Regeneration Research, 9, 555–560.

36. Yassa HA, George SM, Refaiy Ael R and Moneim EM, 2014. *Camellia sinensis* (green tea) extract attenuate acrylamide induced testicular damage in albino rats. Environmental Toxicology, 29, 1155–1161.

37. Zhang P, Pan H, Wang J, Liu X and Hu X, 2014. Telomerase activity-independent function of telomerase reverse transcriptase is involved in acrylamide-induced neuron damage. Biotechnic and Histochemistry, 89, 327–335.

38. Zhao M, Liu X, Luo Y, Guo H, Hu X and Chen F, 2015. Evaluation of protective effect of freeze-dried strawberry, grape, and blueberry powder on acrylamide toxicity in mice. Journal of Food Science, 5, 1750–3841.

The following studies were not considered relevant for the hazard identification and characterisation of AA, and thus not included in the opinion (EFSA CONTAM Panel, 2015) (in alphabetical order according to the first author):

1. Bent G-A, Maragh P, Dasgupta T, Fairman RA and Grierson L, 2015. Kinetic and density functional theory (DFT) studies of in vitro reactions of acrylamide with the thiols: captopril, L-cysteine, and glutathione. Toxicology Research, 4, 121–131.

2. Carlsson H, von Stedingk H, Nilsson U and Tornqvist M, 2014. LC-MS/MS screening strategy for unknown adducts to N-terminal valine in hemoglobin applied to smokers and nonsmokers. Chemical Research in Toxicology, 27, 2062–2070.

3. Ghorbel I, Elwej A, Jamoussi K, Boudawara T, Kamoun NG and Zeghal N, 2015. Potential protective effects of extra virgin olive oil on the hepatotoxicity induced by co-exposure of adult rats to acrylamide and aluminum. Food and Function, 6, 1126–1135.

4. Ji J, Jiang D, Sun J, Qian H, Zhang Y and Sun X, 2015. Electrochemical behavior of a pheochromocytoma cell suspension and the effect of acrylamide on the voltammetric response. Analytical Methods, 7, 478–485.

5. Jiang H, Xiang Y, Hu X and Cai H, 2014. Acrylamide inhibits nerve sprouting induced by botulinum toxin type A. Neural Regeneration Research, 9, 1525–1531.

6. Kang DM and Kim I, 2014. Compensation for occupational neurological and mental disorders. Journal of Korean Medical Science, 29, S59–65.

7. Liu Z-T and Lin A-H, 2014. Dietary Factors and Thyroid Cancer Risk: A Meta-Analysis of Observational Studies. Nutrition and Cancer-an International Journal, 66, 1165–1178.

8. LoPachin RM and Gavin T, 2015. Toxic neuropathies: Mechanistic insights based on a chemical perspective. Neuroscience Letters, 596, 78–83.

9. Omoruyi IM and Pohjanvirta R, 2014. Genotoxicity of processed food items and ready-to-eat snacks in Finland. Food Chemistry, 162, 206–214.

10. Shin S, Moon HI, Lee KS, Hong MK and Byeon SH, 2014. A chemical risk ranking and scoring method for the selection of harmful substances to be specially controlled in occupational environments. International Journal of Environmental Research and Public Health, 11, 12001–12014.

11. Tusnio A, Taciak M, Barszcz M, Paradziej-Lukowicz J, Oledzka I, Wiczkowski W, Szumska M, Pastuszewska B and Skomial J, 2014. Thermal sterilization affects the content of selected compounds in diets for laboratory animals. Journal of Animal and Feed Sciences, 23, 351–360.

12. Wang SY, Wang Y, Jin XW, Zhang Y, Chen JS, Ma WW, Wu YH and Wang C, 2015. A urinary metabolomics study of rats after the exposure to acrylamide by ultra performance liquid chromatography coupled with quadrupole time-of-flight tandem mass spectrometry. Molecular Biosystems, 11, 1146–1155.

13. Williams JR, Rayburn JR, Cline GR, Sauterer R and Friedman M, 2014. Potential protective effect of L-cysteine against the toxicity of acrylamide and furan in exposed *Xenopus laevis* embryos: an interaction study. Journal of Agricultural and Food Chemistry, 62, 7927–7938.

ABBREVIATIONS

AA	Acrylamide
ACHIPIA	Chilean Food Quality and Safety Agency
AGES	Austrian Agency for Health and Food Safety
ANSES	Agency for Food, Environmental and Occupation Health and Safety, former Afssa
AUC	Area under the curve
BDSI	Association of the German Confectionary Industry
BMD	Benchmark dose
BMDL	95 % benchmark dose lower confidence limit
CHOPRABISCO	Royal Belgian Association of the Biscuit, Chocolate, Pralines and Confectionary
CONTAM Panel	EFSA Scientific Panel on Contaminants in the Food Chain
COC	UK Committee on Carcinogenicity of chemicals in food, consumer products and the environment
COT	UK Committee on Toxicity of chemicals in food, consumer products and the environment
CSIC	Spanish National Research Council
DTU	Danish National Food Institute
EC	European Commission
ECF	European Coffee Federation
EFSA	European Food Safety Authority
EU	European Union
EUPPA	European Potato Processor's Association
FDE	FoodDrinkEurope
FPPI	Frozen Potato Products Institute
FFQ	Food frequency questionnaire
GA	Glycidamide
GEMS	Global Environment Monitoring System
Hb	Haemoglobin
HEATOX	European Union-funded project Heat-Generated Food Toxicants: Identification, Characterization, and Risk Minimization
IARC	Institute for Research on Cancer
IPCS	International Programme on Chemical Safety
ISS	Istituto Superiore di Sanità
JECFA	Joint FAO/WHO Expert Committee on Food Additives
LB	Lower bound
LOD	Limit of detection
LOQ	Limit of quantification
MB	Middle bound
MOE	Margin of exposure
NCA	National Coffee Association USA
NFA	National Food Agency of Sweden
NMCC	Norwegian Mother and Child Cohort
NOAEL	No-observed-adverse-effect level
PBPK	Physiologically Based PharmacoKinetic
UB	Upper bound
UK	The United Kingdom
WHO	World Health Organization